

ERUCIC ACID IN FOOD:
A Toxicological Review and Risk Assessment
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SUMMARY

Introduction

Erucic acid is a 22-carbon monounsaturated fatty acid with a single double bond at the omega 9 position. Erucic acid constitutes about 30–60% of the total fatty acids of rapeseed, mustard seed and wallflower seed and up to 80% of the total fatty acids of nasturtium seeds. Erucic acid has also been found in some marine animal oils.

In response to potential safety concerns associated with high dietary exposure to erucic acid (myocardial lipidosis and heart lesions in laboratory rats), efforts were made, using selective breeding, to transfer a low erucic acid trait into agronomically adapted cultivars of *Brassica napus* and *B. campestris*, which are used in the production of rapeseed oils. These varieties of rape were superseded by the canola varieties in the 1980s. Canola varieties have improved agronomic characteristics, such as increased yield and improved disease resistance. By definition, canola refers to *B. napus* and *B. campestris* lines containing less than 2% of the total fatty acids as erucic acid. These canola varieties comprise almost the entire rapeseed crop produced in the world today. In 1997, the erucic acid content of 50% of the Australian canola crop was 0.3% or less of the total fatty acids. The maximum reported erucic acid level was 1.6% of the total fatty acids.

Canola oil has virtually replaced all uses for rapeseed oil and can be used by itself as a salad or vegetable oil. However, it is usually blended with other vegetable oils in the production of margarine, shortening, salad oil and vegetable oil.

Toxicological data

Erucic acid, as a fatty acid, is digested, absorbed and metabolised, for the most part, like other fatty acids. This process involves hydrolysis of the ingested triacylglycerols by the intestinal lipases in the small intestine, absorption of the liberated fatty acids by the intestinal cells, then passage into the circulation via the lymph. The length of the fatty acid, its degree of saturation and the digestibility of the triacylglyceride molecule into which it is incorporated all influence this process. In humans, the digestibility of erucic acid containing triacylglycerols is near maximal (99%), whereas in rats the digestibility is somewhat lower (77%).

Once absorbed, fatty acids are distributed to tissues bound to serum albumin. Fatty acids represent the major fuel source of the heart and skeletal muscles. All cells are capable of oxidising fatty acids and this primarily occurs in the mitochondria, yielding ATP. The process is known as mitochondrial β -oxidation. The peroxisomes are also capable of β -oxidation. Erucic acid, however, like other long chain fatty acids, is poorly oxidised by the mitochondrial β -oxidation system, probably because erucic acid is poorly utilised as a substrate by the β -oxidation enzymes. Heart muscle seems particularly poor at oxidising erucic acid. Furthermore, erucic acid also appears to inhibit the overall rate of fatty acid oxidation, by the mitochondria. In liver, the presence of erucic acid appears to induce the peroxisomal β -oxidation system, leading to a gradual decline in erucic acid accumulation and also reduced inhibition of fatty acid oxidation. This is thought to reduce the influx of erucic acid to the heart. Unmetabolised erucic acid can be found in the faeces.

The human health concern with erucic acid arises from two findings. Firstly, experimental studies have demonstrated an association between dietary erucic acid and myocardial lipidosis in a number of species. Myocardial lipidosis is reported to reduce the contractile force of heart muscle. The occurrence of myocardial lipidosis can be explained by the effect that erucic acid has on the mitochondrial β -oxidation system. Secondly, studies have also demonstrated an association between dietary erucic acid and heart lesions in rats. So far, however, there is no evidence that dietary erucic acid can be correlated to either of these effects in humans. Furthermore, there is no conclusive evidence indicating that the development of myocardial lipidosis is causally linked to the development of myocardial necrosis. However, given what is known about erucic acid metabolism, it seems reasonable to expect that humans would also be susceptible to myocardial lipidosis following exposure to high levels of erucic acid.

All of the available animal studies rely on short term or sub-chronic oral exposure to oils containing various proportions of erucic acid. The most common effect associated with short-term, and to a lesser extent, sub-chronic exposure to these oils is myocardial lipidosis. This effect is observed soon after the commencement of oil feeding and appears to be increased in its severity, in a dose-dependent manner, if erucic acid is present. Clinical signs are typically absent; reduced weight gain only occasionally being correlated with erucic acid dose.

Increased myocardial lipidosis is associated with doses of erucic acid at 1500 mg/kg bw/day in rats, although in nursing pigs this occurs at 900 mg/kg bw/day. Nursing pigs appear to tolerate less erucic acid than adult pigs before myocardial lipidosis is evident, suggesting that the immature myocardium and/or liver may be less able to oxidise long-chain fatty acids. The severity of the observed myocardial lipidosis appears to decline with time. This is most likely due to the induction of the peroxisomal oxidation system in the liver, with subsequent downstream effects on the heart. It is not clear whether this adaptation to the oxidation of long-chain fatty acids by the liver, and possibly also the heart, has any long term adverse consequences.

In pigs and monkeys, there appears to be no other adverse findings that can be associated with erucic acid consumption, other than myocardial lipidosis. In rats, however, the animals typically also develop myocardial necrosis followed by fibrosis, at erucic acid doses of 6600 mg/kg bw/day. It is not apparent from these studies if this necrosis has any long-term effects, although it has been reported that the lifespan of rats exhibiting such lesions is not affected. The male rat appears to be predisposed to the development of this type of heart lesion, particularly in response to the feeding of oils, with or without erucic acid.

No chronic, genotoxicity or carcinogenicity data are available. A single generation reproductive study was performed in rats and guinea pigs where doses of erucic acid up to 7500 mg/kg bw/day were not associated with any adverse reproductive or developmental effects.

In establishing a NOEL for the effects of erucic acid, short-term studies are considered the most appropriate as myocardial lipidosis appears rapidly after only short exposures, and is at its most severe early in the exposure period. The available sub-chronic studies are inadequate for deriving a no-effect level because of the absence of myocardial lipidosis in many of the studies as well as inappropriate dosing regimes. A NOEL of 750 mg/kg bw/day, based on the occurrence of increased myocardial lipidosis at 900 mg/kg bw/day in nursing pigs, is considered appropriate.

A number of human epidemiological studies are available which have attempted to establish if there is any association between dietary erucic acid and the occurrence of heart disease, myocardial lipidosis or erucic acid accumulation in the heart. The studies indicate that erucic acid may occur in human heart muscle in geographic areas where vegetable oils containing erucic acid are consumed. However, the available evidence does not indicate an association between myocardial lesions, of the type observed in rats, or significant myocardial lipidosis, and the consumption of rapeseed oil. None of these studies enable a tolerable level for human exposure to be established.

In the absence of adequate human data, the NOEL of 750 mg/kg bw/day, established for pigs, can be extrapolated to humans in order to establish a tolerable level of human exposure. If an uncertainty factor of 100 (10 for extrapolation to humans, 10 for variation within humans) were applied to this NOEL the tolerable level for human exposure would be 7.5 mg erucic acid/kg bw/day, or about 500 mg erucic acid/day for the average adult. This is regarded as the provisional tolerable daily intake (PTDI) for erucic acid.

Dietary exposure assessment

The majority of exposure to erucic acid comes from canola oil. Other oils, such as high erucic acid rapeseed oil and mustard seed oil, are not widely consumed in Australia or New Zealand.

The estimated dietary intake of erucic acid for high consumers of canola oil, assuming the oil contains erucic acid at the highest reported survey level, is about 350 mg/day. This represents about 86% of the PTDI. For the average consumer, the dietary intake is 124 mg/day or 28% of the PTDI.

Risk characterisation

An association between erucic acid and an increased incidence of myocardial lipidosis in animals has been demonstrated. It is not apparent from human data whether this effect also occurs in humans in response to the consumption of erucic acid. The occurrence of increased lipidosis in animals is generally short lived, the myocardium and liver eventually adapting to the oxidation of erucic acid. The long-term effects, if any, of this adaptation are not known.

A tolerable level of human exposure has been established on the basis of the animal studies. There is a 120-fold safety margin between this level and the level that is associated with increased myocardial lipidosis in nursing pigs.

The dietary exposure assessment has concluded that the majority of exposure to erucic acid by the general population would come from the consumption of canola oil. The dietary intake of erucic acid by an individual consuming at the average level is well below the PTDI, therefore, there is no cause for concern in terms of public health and safety. However, the individual consuming at a high level has the potential to approach the PTDI. This would be particularly so if the level of erucic acid in canola oil was to exceed 2% of the total fatty acids.

INTRODUCTION

Chemical properties

Erucic acid, also known as *cis*-13-docosenoic acid, is an unbranched, monounsaturated fatty acid with a 22-carbon chain length and a single double bond in the omega 9 position.

Sources of exposure

Erucic acid is found in the seeds of the *Cruciferae* and *Tropaeolaceae*. It constitutes 30–60% of the total fatty acids of rapeseed, mustard seed and wallflower seed and it represents up to 80% of the fatty acids of nasturtium seeds. Erucic acid has also been found in some marine animal oils.

In response to potential safety concerns regarding effects associated with high levels of erucic acid (heart lesions in laboratory rats), efforts were made, using selective breeding, to transfer a low erucic acid trait into agronomically adapted cultivars of *Brassica napus* and *B. campestris*. The terms LEAR (low erucic acid rapeseed) and Canbra (Canadian Brassica) were used to identify rapeseed oil from these crops that contained less than 5% erucic acid. These low erucic acid varieties of rape were superseded by other varieties of *Brassica napus* and *B. campestris* in the 1980s having improved agronomic characteristics, such as increased yield and improved disease resistance. The term “canola” is used to describe seed from the varieties of *Brassica napus* and *B. campestris* that contain less than 2% erucic acid in the oil. These canola varieties comprise almost the entire rapeseed crop produced in the world today. In 1997, the erucic acid content of 50% of the Australian canola crop was 0.3% or less of the total fatty acids. The maximum reported erucic acid level was 1.6% of the total fatty acids.

Distribution in foods

Erucic acid is found primarily in rapeseed oils and mustard seed oils. Rapeseed oils, and to a much lesser extent mustard seed oils, are used extensively in foods. Canola oil has virtually replaced all uses for rapeseed oil and can be used by itself as a salad or vegetable oil. However, it is usually blended with other vegetable oils in the production of margarine, shortening, salad oil and vegetable oil. In Canada, which is the major producer of canola oil, it accounts for 72% of the total vegetable oils that are produced. In Australia, canola oil accounts for 26% of the total vegetable oils that are produced. Most of these oils are destined for the domestic market.

REVIEW OF TOXICOLOGY DATA

Background

The toxicity of erucic acid is virtually always considered in the context of the toxicity of rapeseed and mustard seed oils, which can contain high levels of erucic acid. Most humans would be exposed to erucic acid by the inclusion of these oils in the diet. This, however, can complicate the interpretation of the study results, making it difficult to ascertain whether the observed effects are directly attributable to erucic acid, or to some other component (or combination of components) in the oil.

Roine *et al* (1960) were the first to report the toxic effects of rapeseed oil. Rats were fed rapeseed oils at up to 70% of the calorie content of their diet. The rats were reported to have

developed myocarditis. Weanling rats fed high levels of rapeseed oil have also been reported to accumulate fat in the heart muscle after only one day of feeding (Abdellatif and Vles 1970a). The level of fat in the heart muscle of these rats was sometimes found to exceed four times normal values with similar changes also observed in the skeletal muscles. The fat droplets are mainly triglycerides containing a large proportion of erucic acid (Houtsmuller *et al* 1970). The fatty accumulation decreases over time and finally disappears even with continued feeding of rapeseed oil. The fat accumulation is reported to disappear even more quickly if erucic acid is removed from the diet (Kitts 1996). The physiological repercussions of the myocardial infiltration are not entirely clear but have been reported to reduce the contractile force in the heart through the impairment of mitochondrial function and subsequent reduction in ATP synthesis (Sauer and Kramer 1983b). In this respect, myocardial lipidosis can be regarded as an adverse effect, although the long-term implications are unclear given that the effect appears to be reversible, even without removal of erucic acid from the diet. This does not exclude the possibility that the adaptation of the liver and/or myocardium to the oxidation of long chain fatty acids will itself produce long term adverse consequences.

The disappearance of fat accumulation has been reported to be followed by mononuclear cell infiltration, focal myocardial necrosis and eventually myocardial fibrosis in the rat (Abdellatif and Vles 1970a,b). A causal link between myocardial lipidosis and myocardial necrosis, however, has not been conclusively established; it appears that myocardial necrosis occurs spontaneously in male rats in the absence of any observed myocardial lipidosis (Sauer and Kramer 1983a). Rapeseed oil fed at high levels has also been reported to retard growth in the rat, and when fed throughout the lifespan at such levels, causes a high incidence of degenerative changes in the liver, nephrosis, and smaller size and weight of the litters of these animals (Abdellatif and Vles 1970a). The lifespan of these animals, however, is reported to be unaffected, in spite of these degenerative changes.

It has been suggested that the rat is not an appropriate model for determining whether erucic acid may pose a risk to human health (Corner 1983). A number of reasons have been put forward for this. Firstly, most of the rat studies involve feeding oils at a concentration of around 20 % or more by weight in the diet. A level of 20% approximates human lipid consumption. It has been suggested that rats are physiologically incapable of metabolising such concentrations of oil in the diet (Grice and Heggveit 1983). Secondly, there is some evidence that fatty acid metabolism in the rat is dissimilar to that of pigs and primates, making the rat highly susceptible to myocardial lipidosis (Grice and Heggveit 1983). Lastly, focal myocardial necrosis, followed by reparative fibrosis, is a spontaneous idiopathic lesion in the male rat (Corner 1983). The background incidence is reported to be of the order of 17–33% (Goodman *et al* 1979) but it has been suggested that this background incidence is under-reported (Grice and Heggveit 1983). The incidence and severity of these heart lesions can be influenced by the feeding of various marine and vegetable oils but may not be specifically related to the erucic acid content of the oil.

Kinetics and metabolism

Absorption

As erucic acid is a fatty acid, much of this review will concentrate on the general physiological processes for the absorption, digestion and metabolism of lipids and fatty acids.

The digestion of triacylglycerols begins in the small intestine where they are hydrolysed by intestinal lipases to a mixture of free fatty acids and 2-monoacylglycerols. A small fraction of the triacylglycerols remains unhydrolysed. The fatty acids and uncleaved acylglycerols are emulsified by the bile and absorbed by the intestinal cells, where they are largely reassembled into triacylglycerols that enter into the small lymph vessels in the intestinal villi. These highly emulsified triacylglycerols pass from the thoracic duct into the blood via the subclavian vein.

The absorption of fatty acids depends not only on the chain length and degree of saturation but also on the digestibility of the triglyceride molecule into which the fatty acid is incorporated. Digestibility is primarily influenced by the position of the fatty acid in the triglyceride molecule. The absorption of fatty acids is reported to be maximal when they are in position 2 of the triglyceride molecule (Farnworth 1983). Erucic acid, present in high erucic acid rapeseed (HEAR) oil, is nearly always situated in positions 1 and 3 of the triglyceride molecule. Position 2 is mainly occupied by oleic, linoleic or α -linoleic acids.

In humans, the digestibility of erucic acid containing oils is 99% (Deuel *et al* 1949, Vaisey *et al* 1973). In the adult female rat, however, the digestibility of HEAR oil is only 77% (Deuel *et al* 1948). The reason for this difference is not apparent but may reflect interspecies differences in the activities of various lipases. In contrast to the rat, HEAR oil is also reported to be quite readily digestible in pigs with apparent digestibility values similar to those observed in humans (Paloheimo and Jahkola 1959, cited in Sauer and Kramer 1983a). In other animals, such as rabbits and guinea pigs, HEAR oil is reported to have low digestibility, similar to that reported for rats.

Distribution

Free fatty acids become bound to serum albumin and are carried via the blood to other tissues such as the heart and skeletal muscles, which absorb and oxidise free fatty acids as their major fuel source. The rate of uptake of free fatty acids by tissues correlates with the concentration of albumin-bound free fatty acids in the circulation. A large proportion of the initial fatty acid metabolism occurs in the liver, which is particularly efficient at fatty acid uptake from the circulation.

In experiments with rats fed on erucic acid containing oils, the greatest accumulation of erucic acid was noted in the myocardium; the amount of erucic acid being proportional to the amount of erucic acid in the diet (Ziemiński *et al* 1974). In rats fed 30% of their calorie intake from HEAR oil (containing 47% erucic acid), about 34% of the erucic acid was found in the myocardial lipids after 7 days on the diet. This had declined to about 20% after 28 days on the diet. Significant accumulation of erucic acid was also noted in the reserve fatty tissue, the adrenal lipids and in the blood (each containing between 5–15% of the total erucic acid). After long-term feeding of HEAR oil to rats, the amount of erucic acid in the myocardial lipids decreased gradually and at 12 months was reduced to 4.2%. Much less erucic acid (about 2%) was found in the hepatic lipids, suggesting that erucic acid may be more readily metabolised in liver cells.

Metabolism

Almost all cells are capable of metabolising fatty acids. Fatty acids are delivered into cells from two sources. One source is the free fatty acids that arrive via the blood, bound to serum

albumin. The other source is from the breakdown of cell triacylglycerols by the action of lipases.

The degradation and oxidation of fatty acids occurs primarily in the mitochondria. The first step in their metabolism is their transport into the mitochondria. This is a carrier-dependent process using carnitine. Fatty acid molecules are degraded in the mitochondria by progressive release of two-carbon segments in the form of acetyl coenzyme A (acetyl-CoA). This process is known as β -oxidation. The peroxisomes are also capable of performing β -oxidation (Lazarow 1994).

Erucic acid is poorly oxidised by the mitochondrial β -oxidation system (reviewed in Sauer and Kramer 1980). This is because a number of enzymes involved in β -oxidation are inhibited by, or have low activity for, erucic acid. In humans, it has been shown that isolated heart mitochondria metabolise erucic acid more slowly than oleic acid (Clouet *et al* 1974), confirming that rates of erucic acid oxidation are decreased in humans, similar to experimental animals. Not only do the individual enzymes of the mitochondrial β -oxidation pathway have low affinity for erucic acid as a substrate, but the overall β -oxidation rates of other fatty acids are also reduced in the presence of erucic acid. This inhibition of fatty acid oxidation is not unique to erucic acid, but rather is a feature common to very long chain monoenoic fatty acids (Sauer and Kramer 1983b). The inhibitory effect on overall β -oxidation rates is thought to be responsible for the accumulation of lipids in the heart, and to a lesser extent in the liver, following the feeding of HEAR oils.

In liver, the presence of erucic acid appears to induce the peroxisomal β -oxidation system (Lazarow 1994). This leads to greater overall rates of erucic acid oxidation relative to the shorter chain fatty acids, such as oleic and palmitic acid. Oleic and palmitic acid are more easily metabolised by the mitochondrial β -oxidation system (Neat *et al* 1981, Thomassen *et al* 1982). Cardiac tissue, on the other hand, is less able than the liver to oxidise erucic acid, leading to greater relative accumulation of erucic acid in this tissue. The reasons for this are not readily apparent but could be due to a reduced capacity for peroxisomal oxidation in heart tissue.

As the erucic acid concentration in hepatic tissue decreases with induction of the peroxisomal β -oxidation system, the inhibitory effects on the oxidation of other fatty acids decreases. Increased rates of hepatic oxidation by the peroxisomes is thought to lead to a reduced influx of long chain monoenoic fatty acids into the heart, leading to a gradual decline in the lipid accumulation that occurs in that tissue (Sauer and Kramer 1983b). In this respect, it appears as though the liver, and possibly also the myocardium, can adapt to the oxidation of long-chain fatty acids. It is not clear if this metabolic adaptation, itself, has any long-term consequences on the physiology of either the liver or the heart.

Significant interspecies differences are reported to exist in the relative and absolute rates of oxidation of different chain length fatty acids by heart muscle (Sauer and Kramer 1983b). For example, mitochondria isolated from pig heart had threefold greater erucic acid oxidation rates than mitochondria isolated from rat heart (Buddecke *et al* 1976, cited in Sauer and Kramer 1983b). Similar findings have been found between monkey and rat hearts. These findings are probably due to interspecies differences in the enzymes of fatty acid β -oxidation, where differences in physiochemical and chain length specificities of particular enzymes isolated from various species, have been observed (Hall *et al* 1976, cited in Sauer and Kramer 1983b).

Excretion

Rocquelin and Leclerc (1969) demonstrated experimentally that erucic acid accounts for 75–77% of all fatty acids recovered from faeces, where it is excreted as free acid, monoglyceride, or diglycerides. Other experiments have shown that after oral administration of erucic acid in the form of rapeseed oil, or as the ethyl ester, it is eliminated with the faeces over a period of 5 days (Ziemiński *et al* 1973a).

Short-term repeat-dose toxicity

Rats

Groups of male Sprague–Dawley rats (10 rats/group) were fed diets containing 20% by weight fat/oil mixtures with either ~2.5 or ~9% erucic acid (calculated to be 400 and 1500 mg/kg bw/day) for one week (Kramer *et al* 1992). Corn oil (0% erucic acid) and high erucic acid rapeseed oil (43% erucic acid, calculated to be 6900 mg/kg bw/day) were fed as controls. Rats fed the HEAR oil gained significantly less weight relative to the other treatment groups, which had weight gains equivalent to the corn oil fed rats. Hearts were examined histologically for the presence of cardiac triacylglycerol (TAG) and whether erucic acid was a component of the TAG. Heart weights were similar for all groups. Controls rats fed on corn oil exhibited trace myocardial lipidosis. Compared to rats fed corn oil, the incidence and severity was slightly higher in rats fed oils with about 2.5% erucic acid, however, the differences were not significant. Oils with about 9% erucic acid (about 1500 mg/kg bw/day) produced significantly increased myocardial lipidosis compared to rats fed oils with about 2.5% erucic acid. The areas most affected were the right and left ventricles near the base of the heart. In contrast, myocardial lipidosis in HEAR oil fed rats (6900 mg erucic acid/kg bw/day) was very extensive throughout the whole heart. An accumulation of erucic acid in heart lipids was also noted. An increase in cardiac TAG was only observed in those rats fed HEAR oil. Livers were not examined.

Groups of male weanling Charles River rats (15/group) were fed diets containing 0, 2.5, 5, 10, 15 or 20% liquid rapeseed oil (calculated to be equivalent to 0, 750, 1500, 3000, 6000, 12000 mg erucic acid/kg bw/day) or 10 or 20% canbra oil (calculated to be equivalent to 300 or 600 mg erucic acid/kg bw/day) in a 20% fat diet, in which the test oils replaced a 3:1 mixture of lard and corn oil, for 1 week (Beare–Rogers *et al* 1971). The 0 to 5% rapeseed oil levels and the 10 and 20% canbra oil levels (i.e., erucic doses up to 1500 mg/kg bw/day) were not associated with any significant increases in fatty acid accumulation in the heart. Abnormal fat accumulation was observed in the myocardium from 10% rapeseed oil in the diet (3000 mg/kg bw/day) and increased in severity as the percentage of rapeseed oil in the diet was increased. At the highest proportion of rapeseed oil (12000 mg erucic acid/kg bw/day), interstitial oedema, myocytolysis and some focal areas of necrosis were observed in the heart. Livers were not examined.

Groups of weanling Charles River rats (10/sex/group) were fed diets containing 20% of either a 3:1 mixture of lard and corn oil (0% erucic acid), rapeseed oil (33% erucic acid, calculated to be equivalent to 6600 mg/kg bw/day), or partially hydrogenated rapeseed oil (26% erucic acid, calculated to be equivalent to 5200 mg/kg bw/day) (Beare–Rogers *et al* 1971). Rats were killed at 3, 7, 14 or 28 days. Rats receiving the lard/corn oil mixture gained more weight over the period of the experiment. Heart and liver weights did not vary between treatment and control groups. As would be expected, rats receiving the maximum dose of erucic acid accumulated greater amounts of erucic acid in the liver, reaching its peak at 14

days. The accumulated erucic acid declined thereafter and was not significantly different from controls by day 28. The heart accumulated large amounts of fatty acids, with significantly greater amounts being accumulated in those rats fed the rapeseed oil (erucic acid at 6600 mg/kg bw/day) for 1 week. Those fed the partially hydrogenated rapeseed oil (erucic acid at 5200 mg/kg bw/day) also accumulated fatty acids but not to the same degree as those fed the liquid rapeseed oil. By 28 days the level of fatty acids in the heart had declined but was still significantly greater than the fatty acids in hearts of control animals fed the lard/corn oil mixture. Histologically, fat droplets were visible in the myocardium of all rats fed a diet containing erucic acid for 3, 7 and 14 days. After 28 days, only those rats fed the liquid rapeseed oil consistently had abnormal lipid deposition. By 28 days, evidence of necrosis and fibrosis was also observed in the hearts of those rats receiving the liquid rapeseed oil.

Groups of weanling male Sprague Dawley rats (number/group not specified) were fed diets containing 20% HEAR (48% erucic acid, calculated to be 17400mg/kg bw/day) or LEAR oil (1% erucic acid, calculated to be 400 mg/kg bw/day) for 1 or 4 weeks, or a diet of 5% HEAR oil (calculated to be 4300 mg/kg bw/day) for 4 weeks (Lishi *et al* 1991). Controls were fed a basal diet without the addition of any oil. The livers of rats fed a diet containing either 4300 or 17400 mg erucic acid/kg bw/day exhibited fatty degeneration. Liver weights were also increased in these groups. This was assumed by the authors to be the result of fat accumulation in the liver. Liver weight positively correlated with the content of erucic acid in the diet and with the duration of exposure (i.e., were observed at an estimated erucic acid dose of 4300 mg/kg bw/day, but became more pronounced at the higher dose of 17400 mg/kg bw/day). The feeding of HEAR oil to rats was also associated with decreased hepatic capacity for oxidation of palmitic acid (C16), this decrease being less pronounced in those animals exposed for 4 weeks. The authors speculated that the initial suppression of mitochondrial oxidation of other fatty acids is one of the reasons for fat accumulation in the heart and liver which is observed following the feeding of HEAR oils to rats. The study also showed that peroxisomal β -oxidation is induced following the feeding of HEAR oil resulting in enhanced catabolism of erucic acid after continued exposure to the diet. The oxidation of short chain fatty acids (e.g., butyric acid) was not affected by feeding HEAR oil. None of the observed effects were apparent in rats fed LEAR oil (400 mg erucic acid/kg bw/day). Hearts were not examined.

Groups of albino Sprague Dawley rats (8/group, sex not specified) were fed diets containing 10% hydrogenated rapeseed oil, high erucic acid rapeseed oil or low erucic acid rapeseed oil for a period of six weeks (Badawy *et al* 1994). Control rats were fed diets containing 10% corn oil. Crude preparations of high and low erucic acid rapeseed oil were prepared from rapeseed samples for inclusion in the diet. The amount of erucic acid in the oil appears not to have been directly quantified for this study, but was most likely in the range of 20–50% for the high erucic acid rapeseed oil, and 0–5% for the low erucic acid rapeseed oil. It is not possible to estimate the erucic acid dose on the basis of this information. Rats fed a diet of high erucic acid rapeseed oil exhibited reduced body weight gain in comparison to rats fed a diet containing either corn oil or low erucic acid rapeseed oil. This is consistent with the findings of other studies. Growth retardation was also observed in rats fed the hydrogenated rapeseed oil. This may be due to a decrease in the nutritional value of the rapeseed oil resulting from the hydrogenation, which significantly reduces the amount of linolenate and linoleate (Cichon and Rutkowaki 1974, Blomstrand *et al* 1985). Non-significant reductions ($P < 0.1$) in serum total lipids were observed for all groups compared to the controls. Significant decreases ($P < 0.05$) were observed in serum total cholesterol levels in animals fed the hydrogenated rapeseed oil. Non-significant increases in total cholesterol were observed in animals fed either low or high erucic acid rapeseed oil. Serum triglycerides were

significantly increased in rats fed low erucic acid rapeseed oil. The activities of serum glutamic oxaloacetic transaminase, glutamic pyruvic transaminase and alkaline phosphatase were examined and no significant difference were observed between any of the treated or control groups. Histopathological examinations were only done on the liver and kidney. Albuminous degeneration, the presence of fat globules in the hepatocyte, and focal aggregations of mononuclear inflammatory cells were observed in the liver of rats fed hydrogenated rapeseed oil. Mild degenerative changes were also observed in the convoluted tubules of the kidney in these animals. In rats fed the high erucic acid rapeseed oil, vacuolation of hepatocytes and mononuclear aggregation was observed, especially around the blood vessels. Granulomas of mononuclear inflammatory cells and congestion of the central vein were also observed. The kidney tubules revealed degenerative changes and infiltration with mononuclear inflammatory cells. Similar effects were also observed in rats fed low erucic acid rapeseed oil. Histopathological examinations of controls were either not done or not reported, making it impossible to determine if the observed histopathological effects are associated specifically with erucic acid or simply with the feeding of a high fat diet. Hearts were not examined.

Groups of male, weanling Wistar rats (20/group) were fed a diet containing 17.5% corn oil (0% erucic acid), low erucic acid rapeseed oil (1% erucic acid, calculated to be 120 mg/kg bw/day), high erucic acid rapeseed oil (46% erucic acid, calculated to be 5500 mg/kg bw/day), or mustard seed oil (55% erucic acid, calculated to be 6600 mg/kg bw/day) for eight weeks (Watkins *et al* 1995). Body, liver and heart weights did not differ significantly between the different treatment groups. Animals fed the corn oil had the lowest levels of serum cholesterol. The difference in serum cholesterol levels was most significant between the corn and LEAR oil fed animals compared to the HEAR and mustard seed oil fed animals. Circulating triglyceride levels were significantly different between treatment groups but could not be correlated to the presence of erucic acid. Tissue pathology revealed that the feeding of mustard seed oil was associated with myocardial lipidosis accompanied by considerable swelling, seen as oedema of the basal membrane, of the cardiomyocytes. The degenerative changes were characterised by loss of striation and granular cytoplasmic eosinophilia. The mononuclear cell population also appeared slightly increased in the mustard seed oil fed animals. Similar changes were also seen, though to a lesser degree, in the tissues of HEAR oil fed animals. Degenerative or hypertrophic changes were not observed in the LEAR or corn oil fed animals. The feeding of mustard seed oil was associated with increased platelet aggregation. Increased platelet ATP release was also observed in whole blood removed from animals fed mustard seed and HEAR oil but not in whole blood from corn oil fed animals. Livers were not examined.

Pigs

Groups of newborn Yorkshire piglets (3–4/sex/group) were fed milk replacer diets, made up of 25% oil (or about 50% of calories), from birth to two weeks of age (Kramer *et al* 1990). The oil added to the diets contained 0.8, 2.3, 4.7, 7.0, 11.7, 20.7 or 42.9% erucic acid, equivalent to dose levels between about 130–6500 mg/kg bw/day. The growth, and histological and lipid changes in the hearts of the piglets were compared with sow reared piglets. Myocardial lipid infiltration in pigs is reported to be far less noticeable than in rats (Sauer and Kramer 1983a). Myocardial lipidosis in pigs is usually only detectable by chemical stains, which was the method of detection used in this study. Piglets fed the milk replacer diets grew as well as piglets left with the sow. No significant differences were noted in the digestibility of the dietary oils containing differing levels of erucic acid. None of the piglets at birth exhibited myocardial lipidosis prior to nursing. After one day of nursing, 8/10

piglets examined showed myocardial lipidosis. Signs of myocardial lipidosis disappeared by 7 days of age in the nursed piglets. The occurrence of myocardial lipidosis in the newborn piglets is believed to be attributed to the apparent low capacity of the foetus to oxidise fatty acids (Werner *et al* 1983). However, this capacity is reported to increase rapidly after birth. There was a significant correlation of the myocardial lipidosis scores to the content of erucic acid in the diet after 6, 9 and 12 days on the rapeseed oil diet. Increased myocardial lipidosis was noticeable from 900mg/kg bw/day and was greatest in piglets fed in excess of 1100 mg erucic acid/kg bw/day for 4 to 9 days. Piglets fed diets containing 750 mg erucic acid/kg bw/day also exhibited myocardial lipidosis, however, this was not significantly different from what was observed in piglets fed soybean oil (containing 0% erucic acid). Focal myocardial necrosis, which has been reported as a frequent occurrence in rats fed high-erucic acid rapeseed oil (Abdellatif and Vles 1970a,b), was not observed in any of the piglets fed up to 6500mg erucic acid/kg bw/day for 15 days. Livers were not examined.

Groups of piglets (number/group not specified) were fed diets containing HEAR oil (48% erucic acid), fish oil (14.6% erucic acid), partially hydrogenated fish oil (14.3% erucic acid), or a lard/sunflower oil (0 % erucic acid) for 22 days (Opstvedt *et al* 1979, cited in Corner 1983). After 10 days of feeding, a mild to moderate cardiac lipidosis was observed in piglets fed diets containing 2% by weight or more erucic acid (presumably the HEAR oil diet), but there were no differences between the refined fish oil and partially hydrogenated fish oil. Livers were not examined.

Four-week-old Yorkshire piglets (4/group, sex not specified) were fed a diet of corn-soybean meal containing 10% rapeseed oil (about 0.4% erucic acid content) for eight weeks (Cullen *et al* 1996). A control group was fed the same base diet containing 10% fat (source of fat not specified). The liver of control animals appeared normal. A number of ultra structural changes in the liver parenchymal cells of rapeseed oil-fed animals were observed, including abnormal bile canaliculi and mitochondria, and augmentation of smooth endoplasmic reticulum profiles and peroxisome numbers. Liver peroxisomes have been shown to catalyse the β -oxidation of fatty acids in rats (Lazarow 1994), therefore, an increase in peroxisome numbers may be an adaptive response by the liver to large amounts of fatty acids in the diet. Hearts were not examined.

Monkeys

Eleven cynomolgus monkeys (*Macaca fascicularis*) were fed diets containing an added 25% of a mixture of 3:1 lard and corn oil or HEAR oil (23% erucic acid, calculated to be about 3000mg/kg bw/day) for 120 days (Schiefer *et al* 1978, cited in Kramer and Sauer 1983a). Fatty infiltration of the myocardium was apparent in both treatment groups but was greater in those animals fed the HEAR oil.

Conclusion

The heart appears to be the principal target organ for toxic effects following short-term exposure to edible oils containing erucic acid. The most common observed effect, among rats, pigs and monkeys, is myocardial lipidosis. Studies in rats and young pigs demonstrate a dose relationship between the level of erucic acid in the diet and severity of myocardial lipidosis. Clinical signs are typically absent; reduced weight-gain only occasionally being correlated with erucic acid dose. The accumulation of lipids in the heart may be due to a reduced capacity to oxidise very long chain fatty acids, such as erucic acid. The myocardial lipidosis appears to decline in severity with time. This is most likely due to the induction of

the peroxisomal oxidation system in the liver, with subsequent downstream effects on the heart. It is not clear whether this adaptation to the oxidation of long-chain fatty acids has any long-term adverse consequences. In nursing pigs, increased myocardial lipidosis is associated with erucic acid doses of 900 mg/kg bw/day (a dose of 750 mg/kg bw/day is not associated with any observed effect). In rats, increased myocardial lipidosis is observed at doses of 3000 mg/kg bw/day (a dose of 1500 mg/kg bw/day is not associated with any observed effect).

In rats, there also appears to be a dose relationship between erucic acid and the occurrence of heart lesions. These lesions are evident from erucic acid doses of 6600 mg/kg bw/day for 4 weeks (a dose of 5200 mg/kg bw/day is not associated with any observed effect). In piglets, heart lesions are not observed at doses of erucic acid up to 6500 mg/kg bw/day. Fatty and degenerative changes in rat liver have also been observed at erucic acid doses from 4300 mg/kg bw/day.

Sub-chronic toxicity

Pigs

Groups of male and female pigs (6/sex/group) were fed soybean oil or LEAR oil (4.3% erucic acid) at 10 and 20% by weight of their diet (estimated to be equivalent to 170 and 340 mg erucic acid/kg bw/day, respectively) for periods of 1, 4 and 16 weeks (Friend *et al* 1975a, cited in Corner 1983). Trace lipidosis was demonstrated by staining in some hearts of all treatment groups at most time intervals. The results indicate that a slightly greater number of pigs (statistical significance not reported) fed the 20% fat diets, than those fed the 10% fat diets, had myocardial lipidosis. Slightly greater numbers of pigs fed the 20% LEAR oil (18/36 pigs) were affected with myocardial lipidosis than those fed the soybean oil (13/36 pigs), although the severity of the lipidosis was the same between treatment groups. Minute focal interstitial infiltrations of mononuclear cells were found in all treatment and control groups including the controls killed at day 0. Foci of overt myocardial necrosis were not observed in any of the treatment or control groups.

Groups of Yorkshire boars (24/group) were fed a diet containing 20% by weight of soybean oil (0% erucic acid) or HEAR oil (22.3% erucic acid, calculated to be equivalent to 1800mg/kg bw/day) for 16 weeks (Friend *et al* 1975b, cited in Kramer and Sauer 1983a). Controls were fed a no oil diet. The incidence of heart lesions was low in all groups (1/24 no oil, 1/24 soybean oil, 3/24 HEAR oil). The slightly increased incidence of heart lesions in the HEAR oil group was not statistically significant. Myocardial lipidosis was not evident in any of the boars examined.

Groups of Yorkshire boars (15/group) were fed diets containing 20% by weight of corn oil, LEAR oil (0.9% erucic acid, calculated to be equivalent to 70 mg/kg bw/day), or HEAR oil (24% erucic acid, calculated to be equivalent to 2000 mg/kg bw/day) for up to 24 weeks (Friend *et al* 1976, cited in Kramer and Sauer 1983a). Controls were fed a no oil diet. No significant differences between treatment groups and the controls were noted in the incidence and severity of heart lesions. The incidence of myocardial lipidosis was not reported.

Groups of crossbred pigs (16/group, sex not specified) were fed diets containing 15% rapeseed oil comprising 0.3, 1.2, 4.9, or 34.2% erucic acid content (calculated to be 2, 100, 400, or 2800 mg/kg bw/day), or a control diet to which no oil was added, for a period of up to 23 weeks (Aherne *et al* 1976). Four pigs from each of the five treatments were killed at 4

weeks, eight at 16 weeks and the remaining four at 23 weeks. Serum cholesterol levels were significantly elevated in all animals that received oil in the diet, irrespective of the erucic acid concentration. Serum glutamic oxaloacetic transaminase activity was significantly elevated in some animals but this could not be correlated to the presence or dose of erucic acid. Measurements of the pig carcass “fatness” were significantly affected by the addition of rapeseed oil to the diet, but once again could not be specifically correlated to erucic acid, indicating that this effect may be associated with some other component of the oil. Fat accumulation could not be detected in the myocardium of any of the pigs. Myocardial necrosis was detected in 5 out of the 80 pigs used in the experiment, but three of these animals had been fed the control diet, therefore this effect could not be correlated with the presence of erucic acid in the diet.

Groups of female landrace pigs (number/group not specified) were fed diets containing HEAR oil, fish oil, partially hydrogenated fish oil, partially hydrogenated soybean oil or lard (proportions of erucic acid not specified) for periods up to 1 year (Svaar *et al* 1980, cited in Corner 1983). A mild cardiac lipidosis, as determined from staining, was observed in a few pigs fed on the partially hydrogenated fish oil and the HEAR oil for 1, 5 and 27 weeks. Minor heart lesions consisting of small foci or individual muscle cell necrosis were found after 1 week and more frequently after 6 months and 1 year. There was no relationship between the incidence and severity of the heart lesions and any particular type of fat in the diet.

Monkeys

Groups of cynomolgus monkeys (1–3/sex/group) were fed on diets containing an added 25% of a mixture of 3:1 lard and corn oil or HEAR oil (21% erucic acid, calculated to be about 2600mg/kg bw/day) for up to 30 months (Schiefer 1982, cited in Kramer and Sauer 1983a). Monkeys were killed at 6, 12, 18, 24 and 30 months. The results were similar to the finding of an earlier experiment (Schiefer *et al* 1978, cited in Sauer and Kramer 1983a). Fatty infiltration of the myocardium was apparent in both treatment groups but was greater in those animals fed the HEAR oil, although the lard/corn oil fed group also had significant myocardial lipidosis at 6 and 12 months. This decreased thereafter. When the heart tissue was examined with the electron microscope, monkeys fed on the HEAR oil had enlarged and irregularly shaped mitochondria. Some deterioration of the mitochondrial cristae was also observed. The presence of myocardial lesions was not reported.

Conclusion

The heart appears to be the principal target organ following sub–chronic exposure to edible oils containing erucic acid, at least in pigs and monkeys, although the effects appear to be less pronounced than those observed following short term exposure. Overall in pigs, significant myocardial lipidosis does not appear to be associated with erucic acid doses up to 2800 mg/kg bw/day. It appears, on the basis of this data, that adult pigs are able to tolerate greater levels of erucic acid than young pigs (compare short–term studies). This suggests that the immature myocardium and/or liver may be less able to metabolise long–chain fatty acids, making neonates especially prone to myocardial lipidosis, albeit transiently. Monkeys appear to be more susceptible than pigs to the development of myocardial lipidosis following the feeding of HEAR oil. Myocardial necrosis does not appear to be associated with sub–chronic exposure to erucic acid in either pigs or monkeys.

Chronic toxicity

No chronic toxicity studies were available.

Developmental/reproductive toxicity

Groups of male and female weanling Wistar rats and weanling Golden Syrian hamsters were fed diets containing either 25% rapeseed oil (41.5% erucic acid, calculated to be about 7500 mg/kg bw/day) or corn oil (0.5% erucic acid, calculated to be about 100 mg/kg bw/day) for a period of 90 days prior to mating (Reyes *et al* 1995). About 50% of the females were then randomly selected for mating with males receiving an identical diet. Pregnant rats and hamsters were then continued on the same diet until the end of pregnancy, with the non-pregnant controls also receiving the same diet. Studies were done on the last day of pregnancy; day 20 in the rat and day 14 in the hamster. Animals were weighed, bile was collected and liver, heart and kidneys were weighed and examined, and samples taken for fatty acid analysis. In pregnant animals, the fetuses were counted and weighed. Mating was successful for both rats and hamsters with all pregnancies reaching full term. There were no significant differences in the number of fetuses or fetal weight in rats or hamsters fed either rapeseed or corn oil. Gross morphological abnormalities were not observed in any of the fetuses. Weight gain was lower in non-pregnant rats and hamsters fed rapeseed oil, however, no significant differences were detected in liver, heart, or kidney weight. In pregnant rats and hamsters the body weight gain was similar with both dietary oils. No evidence of inflammation, necrosis or fibrosis was detected in the liver, heart, kidneys or adrenals with either oil. Mild myocardial lipidosis was observed in pregnant hamsters fed both oils. The greatest deposition of erucic acid in rats fed rapeseed oil for 130 days occurred in the adrenals, with decreasing amounts found in the plasma, heart, spleen, kidney, liver, erythrocytes, testis, and brain. The proportionally greater accumulation of erucic acid in the heart is believed to reflect a peroxisomal oxidative capacity that is low relative to that in liver and kidney. No hepatic functional abnormalities were detected in any of the treatment groups. Bile flow and biliary lipid composition were similar in non-pregnant and pregnant animals fed regardless of the dietary oil.

Conclusion

The feeding of a diet containing up to about 7500 mg erucic acid/kg bw/day to hamsters and rats for 90 days prior to mating, and continuing until the last day of pregnancy was not associated with any apparent adverse reproductive or developmental effects. In addition, the occurrence of mild myocardial lipidosis in the hamsters appeared not to be correlated specifically with the presence of erucic acid in the diet. These findings contrast to those obtained with rats in the short-term studies, perhaps suggesting that pregnancy may increase the rates of fatty acid metabolism, making the animals less predisposed to develop myocardial lipidosis.

Carcinogenicity

No carcinogenicity studies were available.

Genotoxicity

No genotoxicity studies were available.

Effects in humans

The potential for erucic acid to produce toxic effects in the human heart, leading to increased incidence of heart disease, has been the subject of much speculation. Focal myocardial lesions, of the type described for the rat, are sometimes found incidentally in human hearts. However, the aetiology of these lesions is different, often resulting from low-grade infectious myocarditis, drugs, poisons, and clinical conditions known to cause diffuse or multifocal myocardial necrosis in humans. There does not appear to be any evidence that dietary fat consumption is a factor in any of these conditions (McKinney 1974, cited in Grice and Heggveit 1983).

A number of studies of humans are available concerning the accumulation of erucic acid in the human myocardium as related to diet, the occurrence of lipidosis in humans, and the incidence of cardiomyopathy in humans and its relationship to diet. The following studies are considered relevant.

A study initiated by the Indian Council of Medical Research and reported in the Annual Report of the National Institute of Nutrition, Hyderabad, India (Anon 1976,1977, cited in Grice and Heggveit 1983), indicated that levels of erucic acid in the myocardium are related to the vegetable oils principally consumed in the particular district studied. In Calcutta, mustard seed oil high in erucic acid (40–44 %) is the main edible oil; in Madras, peanut and sesame oil are the principal edible oils; and in Trivandrum, coconut oil is the primary edible oil. Over 100 hearts from the Calcutta region, 38 from Madras and 25 from Trivandrum were examined. In the mustard seed oil consuming centre of Calcutta, significant amounts of erucic acid were detected in the myocardium (range of 0.9–9.9%), whereas in the other two regions there were no detectable amounts of erucic acid in myocardium, suggesting that dietary erucic acid intake is reflected in the levels of fatty acids in the myocardium. The presence of significant amounts of erucic acid in the myocardium could not be associated with any observed heart damage.

France, like India, is a major consumer of rapeseed oil. An epidemiological study conducted in France in 1974 indicated that of 254,788 cases of death, due to heart failure, 269 cases, or 0.11%, were identified as a cardiomyopathy somewhat similar in histology to the observed cardiomyopathy in rats (Chone 1977, cited in Grice and Heggveit 1983). Of the 269 cases, a significant association with alcohol consumption was found, but none could be established with dietary fat and vegetable oil consumption.

In a study by Svaar (1982) the accumulation of erucic acid was examined in the hearts of 54 Norwegian men, aged 20 to 69, who had died suddenly from accidents. These hearts were selected from a larger group on the basis of being without myocardial infarction, severe coronary stenosis, cardiac hypertrophy or valvular disease by macroscopical examination. No focal myocardial lesions were present. A mild to moderate lipidosis was found in 50% of the hearts but this could not be correlated with the concentration of erucic acid in the myocardium, which was present at less than 1% of the total lipids.

In May 1981 in Spain, hundreds of people died and thousands were poisoned by the consumption of rapeseed oil (McMichael 1981). Erucic acid has been implicated, by some, as the causative agent for this “toxic oil syndrome” (James 1994). Chemical analyses of samples of the oil obtained from families who fell ill revealed that the oil was, in fact, a mixture of industrial rapeseed oil, soybean oil, olive oil, and animal fats that had been purposely denatured with 2% aniline and was never intended to be used as an edible oil

(Tabeunca 1981, Gollob 1981). When the oil was heated, toxic anilides would be formed. Anilides are reported to have been found in the fatty tissues of victims (Gollob 1981). The aetiology of the "toxic oil syndrome" has not been conclusively established, however, the disease appears to have two clinical phases, one with pneumonia like symptoms, and the second with similarities to autoimmune disease in which neuromuscular changes predominate (Gilsanz 1982). A syndrome, similar to the "toxic oil syndrome" has been reproduced in animal models fed mixtures of oleyl and linoleyl anilides (Tena 1982). It seems doubtful that this syndrome is related specifically to rapeseed oil or its erucic acid component.

Conclusion

Heart lesions, similar to those seen in rats, are observed in humans; however, they are usually attributed to other, specific causes. The available studies in humans indicate that erucic acid may occur in human heart muscle in geographic areas where vegetable oils containing erucic acid are consumed. However, the available evidence does not indicate an association between myocardial lesions, of the type observed in rats, or significant myocardial lipidosis, and the consumption of rapeseed oil.

HAZARD CHARACTERISATION

Establishing a NOEL in animals

Only sub-chronic and short-term feeding studies are available. The most sensitive indicator of an effect associated with the short-term, and to a lesser extent, sub-chronic feeding of oils to animals appears to be myocardial lipidosis. This effect is observed very shortly after the commencement of feeding and appears to be increased in its severity, in a dose-dependent manner, if erucic acid is present. The severity of the lipidosis appears to decline with time regardless of whether or not the feeding of erucic acid continues. In this respect, myocardial lipidosis can be regarded as a short-term, reversible effect. In rats, high erucic acid doses also appear to be associated with the occurrence of myocardial necrosis. However, a causal link between myocardial lipidosis and myocardial necrosis has not been conclusively established.

The available sub-chronic studies are not adequate for deriving a NOEL because of the absence of myocardial lipidosis in many of the studies, as well as inappropriate dosing regimes. As myocardial lipidosis appears rapidly after only short exposures, and is also at its most severe early in the exposure period, it is appropriate in this instance to use the data from short-term studies to establish the NOEL.

In rats, the NOEL is 1500 mg/kg bw/day on the basis of increased myocardial lipidosis at 3000 mg/kg bw/day. However, in nursing piglets, the NOEL is lower at 750 mg/kg bw/day on the basis of increased lipidosis at 900 mg/kg bw/day.

An overall NOEL of 750 mg/kg bw/day is, therefore, considered appropriate based on short-term studies in the pig.

Establishing a tolerable level of exposure for humans

A number of epidemiological studies on the consumption of oils containing high levels of erucic acid exist. These do not indicate any association between erucic acid and the occurrence of heart disease. The occurrence of myocardial lipidosis in humans cannot be

directly commented on, as it has not been associated with erucic acid in the diet, or the consumption of rapeseed oils. In animals, this effect is most pronounced shortly after exposure commences. Presumably, in humans exposed to high levels of erucic acid, the myocardium would adapt over time to the oxidation of long chain fatty acids, therefore evidence of myocardial lipidosis would not necessarily be apparent upon examination. None of the human studies are appropriate for establishing a tolerable level for human exposure.

In the absence of adequate human data, the NOEL, established for animals, can be extrapolated to humans in order to establish a tolerable level of human exposure. An uncertainty factor of 100 (10 for extrapolation to humans, 10 for variation within humans) is considered appropriate. Therefore, a tolerable level for human exposure would be 7.5 mg erucic acid/kg bw/day (approximately 500 mg erucic acid/day for the average adult).

DIETARY EXPOSURE ASSESSMENT

Levels in food

Survey data in Australia/New Zealand

The median erucic acid content of the 1997 Australian canola crop was 0.3% of the total fatty acids (3 g/kg) (Mailer *et al*, 1997). The mean erucic acid content was 1.0% and the maximum reported erucic acid content was 1.6%. Higher erucic acid content is generally found in canola grown in Western Australia.

Survey data from overseas

Recent survey data from overseas was not available. However, in oil extracted from the 1986–88 rapeseed crops in the United Kingdom, the mean content of erucic acid was 0.2% of the total fatty acids, with a maximum content of 2.7%. The majority of the oils tested, however, did not contain any detectable erucic acid. The mean erucic acid content of Canadian canola oils in 1984–89 was 0.3–0.6% of the total fatty acids.

Exposure estimates

Limitations in the survey data

The survey data used in the dietary exposure assessment is obtained from Australian canola only.

Exposure estimate for adults/children

Dietary modelling was done to estimate the amount of erucic acid in the diet. It was assumed in this modelling that the majority of the exposure to erucic acid would come from the consumption of canola oil and products containing canola oil, as other sources of erucic acid, such as mustard seed oils are rarely consumed in Australia and New Zealand. Modelling was done using both the median and maximum reported survey levels of erucic acid in the 1997 canola crop. The results appear in the table below:

Estimated dietary exposures to erucic acid from canola oil

	Mean for all respondents	Mean for consumers only	95 th percentile consumers
Maximum survey level (1.6%)			
mg/day	21.3	124.2	348.2
%PTDI ¹	4.8	27.7	85.7
Median survey level (0.3%)			
mg/day	3.9	23.3	65.3
%PTDI	0.9	5.2	16.1

¹ PTDI 7.5mg erucic acid/kg bw/day

Estimated dietary exposures to erucic acid from canola oil are below the PTDI for mean as well as high consumers.

Individuals would only be likely to exceed the PTDI if the level of erucic acid in canola oil exceeded 2% of the total fatty acids.

RISK CHARACTERISATION

Severity of toxicological endpoint and limitations in data

Erucic acid has been shown to be associated with an increased incidence of myocardial lipidosis in animals. This is probably due to the reduced capacity of the liver and myocardium to oxidise long chain fatty acids. Overt clinical signs in the animals are generally absent, however. The lipidosis occurs very early in the exposure period and decreases over time as the myocardium and liver adapt to the oxidation of erucic acid. Eventually, the lipidosis disappears even with continued exposure to erucic acid. The long-term effects, if any, of this adaptation to the oxidation of long chain fatty acids are not known. Data on the effects of erucic acid on the human myocardium are lacking, and thus far an association between the consumption of rapeseed oil and increased myocardial lipidosis or heart disease has not been established for humans.

Adequacy of the dietary exposure data

The survey data on the levels of erucic acid in canola grown in Australia is extensive. Dietary exposure to erucic acid was estimated on the basis that the vast majority of exposure would come from canola oil, and products such as margarines that contain canola.

Identification of “at risk” groups

At risk groups would be those that are likely to consume significant amounts of high erucic acid rapeseed oil or mustard seed oil.

Estimate of the margin of safety

There is a 120-fold margin of safety between the PTDI and a level of intake of erucic acid that has been associated with increased myocardial lipidosis in pigs.

Conclusion

Evidence presented here supports the conclusion that there is no cause for concern, in terms of public health and safety, with the current mean dietary intakes of erucic acid in canola oil by Australian and New Zealand consumers. High consumers of canola oil, however, have the potential to approach the PTDI.

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