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Role of Conjugated Linoleic Acids in Cancer

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1. INTRODUCTION

Cancers are the second leading cause of deaths, among both women and men. Breast cancer is the malignancy most frequently diagnosed in women. It is also the second most common cause of cancer deaths among women. Although the etiology of most cases of this disease is not known, risk factors include a variety of nutritional factors. The amount of fat consumed in the diet and the quantity and quality of fatty acids (FAs) are especially crucial. Among FAs to which great importance in modification of cancer risk is recognized are conjugated linoleic acids (CLAs). The CLAs are a group of positional and geometric isomers of linoleic acid (LA), with a conjugated double bond system in the carbon chain. The main natural source of CLA is milk and dairy products and meat of ruminants, in which cis-9, trans-11 octadecadienoic acid (rumenic acid) occurs in the largest quantities, constituting over 90% of the total pool of CLA. Another important isomer is trans-10, cis-12 octadecadienoic acid, which occurs with rumenic acid in dietary supplements, usually in the ratio 1:1. Their possible health promoting effects in obesity, atherosclerosis, cardiovascular diseases (CVDs), osteoporosis, diabetes, insulin resistance, inflammation, and various types of cancer, especially breast cancer [1]. The CLAs are octadecadienoic acids (18:2). Interests in CLAs were found to be associated with a number of physiological and pathological responses such as cancer, metastases, atherosclerosis, diabetes, immunity, and body fat/protein composition. The main sources of these CFAs are dairy fats. Rumen bacteria convert polyunsaturated fatty acids (PUFAs), especially LA and linolenic acids, to CLA and numerous trans- containing mono- and diunsaturated FAs. An additional route of CLA synthesis in ruminants and monogastric animals, including humans, occurs via delta9 desaturation of the trans-18:1 isomers. To date, a total of 6 positional CLA isomers have been found in dairy fats, each occurring in 4 geometric forms (cis, trans; trans, cis; cis, cis; and trans, trans) for a total of 24. The analytical techniques are required to evaluate the purity of CLA preparations, because their purity will affect the clarification of any physiological and/or biochemical response obtained. The availability of pure CLA isomers will permit the evaluation and analysis of individual CLA isomers for their nutritional and biological activity in animals and humans model systems. These techniques are also necessary to evaluate dairy fats for their content of

specific CLA isomers and to help design experimental diets to increase the level of the desired CLA isomers in dairy fats. These techniques are also required to evaluate the CLA profile in monogastric animals fed CLA preparations for CLA enrichment of animal products. This is particularly important because absorption and metabolism will alter the ingested-CLA profile in the animal fed [2]. The CLA is present in milk products and meat from ruminants, appears to have anticancer activity against breast cancer. Few epidemiologic data are available in humans. The relation between intakes of CLA, other FAs and breast cancer incidence, CLA-containing food groups are (eg, butter, cheese, milk, other milk products, and meat). CLA intake showed a weak, positive relation with breast cancer incidence. The positive associations were found with total trans FAs and (borderline) with saturated FAs. Significant inverse associations were found with monounsaturated (MUFAs) and cis unsaturated FAs, whereas total fat and energy intake of CLA-containing food groups were not related to breast cancer incidence. The suggested anticarcer property of CLA in animal and tissue culture models could not be confirmed in this epidemiologic study in humans [3]. The CLAs, a mixture of isomers of LA, has many beneficial effects, including decreased tumor growth in animal cancer models. The cis-9, trans-11 isomer of CLA (CLA9,11) can be formed in the rumen as an intermediate in biohydrogenation of LA. The data indicated that tissue desaturation of trans-FAs is an important source of CLA9,11 in milk [4]. Cancer models utilize massive doses of carcinogen so that investigations of anticancer effects require equally large doses. CLAs, consumed in dairy products, are thought to be as anticancer. The naturally produce a CLA-enhanced butter for use in biomedical studies with animal models. The cows fed a low forage diet supplemented with sun-flower oil. This resulted in increases in content of CLA of milk fat, but the markedly high concentrations were transient and declined over a 3-wk period. By collecting milk fat over the first few days on the diet and selecting cows with the greatest CLA concentrations, we were able to produce a butter in which CLA content was enhanced sevenfold over control butter and the cis-9, trans-11 isomer predominated (91%). Thus, butter produced by this method can be used to investigate the preventive role of CLA in natural foods with biomedical models of different types of cancer. Furthermore, the butter allows examination of the other beneficial health effects of CLA reported with animal models [5]. Trans FAs are formed by partial hydrogenation of vegetable and marine oils or by bacterial activity in the rumen of ruminants. Main dietary sources are margarine, meat, milk fat and bakery products. Unsaturated FAs in the trans form have a more straight structure than their cis counterparts. They therefore have properties more like saturated FAs. Trans FAs may compete with essential FAs for elongating and desaturating enzymes and thereby interfere in the formation of eicosanoids. Trans FAs in the diet will increase LDL-cholesterol but to a lesser degree than the SFAs C12-C16. They also decrease HDL-cholesterol and increase Lp(a). By these unfavorable effects on blood lipids it may be expected that they will increase the risk of coronary heart disease. This has been confirmed in some studies, but not all. The diet contains sufficient amounts of essential FAs there are no strong indications that trans FAs may have other unfavorable effects on health. The health effects of such an intake must be considered minor compared to an eight to ten fold higher intake of SFAs [6]. The roles of eicosapentaenoic acid and possibly docosahexaenoic acid, there are two other major important, features of the traditional Eskimo staple diet that contains the UFAs cis oleic, cis LA and cis α-LA as well as their respective metabolites in physiologically optimal concentrations and, it is virtually totally devoid of unnatural and potentially hazardous trans and cis isomers of these FAs. Large quantities of unnatural trans and cis isomers of UFA are found in the Western diet as partially hydrogenated UFA in many foods. These isomers are formed during the manufacture of margarines and related compounds, as food contaminants during excessive heating of cooking oils for deep-frying and other excessive heat-requiring mass food preparation procedures and the excessive feeding with an unnatural diet of ruminants and non-ruminants for increased meat and/or milk production and of poultry for increased egg and/or meat production. These isomers have been shown to display potentially hazardous metabolic effects which include the competitive inhibition of UFA metabolism at various steps and have been causally implicated in the etiology of ischemic heart disease (IHD) and cancer. The myth of the safety of trans FAs arises from misinterpretation of the observation that increasing dietary cis LA reduces the toxic effects of trans UFA. The decrease of 20% in the IHD mortality is directly related to a shift in the dietary ratio of unnatural trans and cis UFA isomers: cis LA in favour of the latter. This ratio will be found to correlate with IHD patterns. Moreover the

proportionality of cis UFA and their metabolites in the diet would render gross tissue UFA utilization relatively independent of desaturase enzyme activity. These enzymes would function to make the minute, critical UFA metabolic adjustments required to ensure the presence of structural UFA in membranes in functionally optimal quantities and, ensure the synthesis of eicosanoids from dihomo-γ-linolenic acid, arachidonic acid and eicosapentaenoic acid in balanced, optimal physiological concentrations for the genetic make-up [7].

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