Available online at www.pharmaresearchlibrary.com

Pharma Research Library
International Journal of Medicine and Pharmaceutical Research
2013, Vol.1 (2): 258-261

ISSN 2321-2624

Review Article

A Substancial and Significant Fruit-Pomegranate

Amit Parashar[1*], Poonam Sharma[2], Satish Goyal, Ashok Kumar[4]

[1, 2] Department of Chemistry, Hardayal Technical Campus, Mathura, India
[3]Vetnairy college, Mathura, UP, India
[4] St John's, College, Agra, India
*E-mail: parashar.amit1@gmail.com

Abstract

Conjugated fatty acids (CFAs) are a mixture of positional and geometric isomers of polyunsatu rated fatty acids with conjugated double bonds. Reports indicate that CFAs have potent beneficial effects, including antitumor, antiobese, antiatherogenic and antidiabetic activities. The molecules have also been shown to prevent the onset of hypertension. Recent reports suggest that each CFA isomer has different functions, for example the 10trans; 12cis isomer of conjugated linoleic acid (CLA) has anticarcinogenic, antiobese and antidiabetic effects, whereas the 9cis, 11trans-CLA iso-mer exerts an anticancer effect. Although it would be interesting to know the effects of CFAs on humans, there are only few reports concerning the anticancer and antiobese effects of CLA in humans. More detailed evaluations of the physiological bioactivities of CFA isomers on lifestyle related desires in humans and animals will be of great interest in future studies.

Key words: conjugated fatty acids, cancer, obesity, hypertension, lifestyle-related diseases

Introduction

Lifestyle-related diseases, such as obesity, hyperlipidemia, Arteriosclerosis, diabetes mellitus and hypertension, are wide spread and increasingly prevalent in industrialized countries. Because of the rapid increase in the number of elderly people, these diseases are important medically and socioeconomically. It is also assumed that one-third of human cancers is associated with dietary habits and lifestyle (1). Although the pathogenesis of lifestyle-related diseases is complicated and the precise mechanisms underlying their development have not yet been elucidated, it has been noted that the quality of dietary lipids could be an important modulator in terms of the morbidity and mortality of

these diseases (2). In particular, polyunsaturated fatty acids (PUFAs), such as linoleic acid (18 : 2, n-6), α-linolenic acid (LNA, 18 : 3, n-3) and arachidonic acid (20 : 4, n-6), are very important for the maintaining biofunctions in mammalians as essential fatty acids (3). In addition, it has been reported that the consumption of n-3 highly unsaturated fatty acids, such as eicosapentaenoic acid (EPA, 20 : 5, n-3) and docosahexaenoic acid (DHA, 22 : 6, n-3), correlates with a reduced risk of cancer and cardiovascular disease in human and animal studies (4, 5).At present, conjugated fatty acids (CFAs) have attracted considerable attention because of their potentially beneficial biologic effects of attenuating lifestyle-related diseases (6-8). CFAs refer to a mixture of positional and geometric isomers of PUFAs with conjugated double bonds. Theoretically, a number of CFA isomers are possible, with multiple Combinations of numerical, positional and geometrical configurations of conjugation in double bonds (Fig. 1).

Natural sources and industrial Production of CFAs

Conjugated linoleic acid (CLA), the CFA form of linoleic acid, has been detected in milk fat, cheese and ruminant meat (9). The 9cis,11trans (9c,11t)-CLA isomer is naturally produced through the biohydrogenation of unsaturated fatty acids by the rumenal bacterium Butyrvibrio fibrisolvens in ruminants, such as cows, sheep, goats and camels (10, 11). The daily intake of CLA has been calculated for various countries and estimated at several hundred mg in a typical diet (12-16). There are also other types of CFA in some plant seed oils. Punicic acid (9c, 11t, 13c-conjugated linolenicacid [CLN]) in pomegranate seed oil, α-eleostearic acid (9c,11t,13t-CLN) in Black berry oil and Muscat seed oil, catalpic acid (9t,11t,13c-CLN) in Alandi seed oil, and calendic acid (8t,10t,12c-CLN) in pot marigold seed oil are present at about72%, 60% to 70%, 31%, and 33%, respectively(Table 1) (17, 18). It has been reported that several seaweeds contain conjugated trienoic and tetraenoic fatty acids. Red seaweed, Ptilota filicna, contains 5t,7t,9t,14c,17c-conjugated EPA (CEPA) and 5c,7t,9t,14c-CEPA, and Bossiella orbigniana contains 5c,8c,10t,12t,14c-CEPA (19, 20). Stellaheptaenoic acid, 4c, 7c, 9t, 11t, 13c, 16c, 19c-conjugated docosaheptaenoic acid, is present in the green seaweed anadyomen stellete.

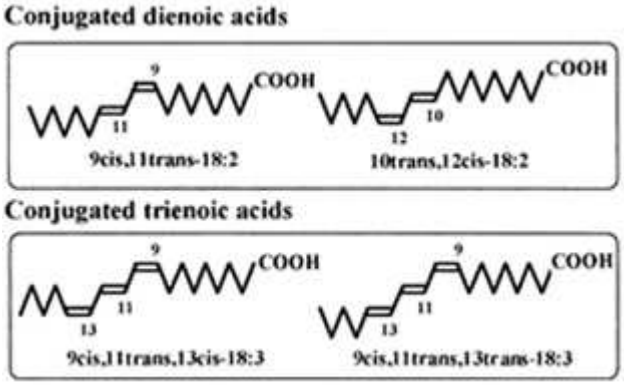

Fig.1. Structure of conjugated fatty acid isomers

Commercial CLA is produced by alkaline isomerization of linoleic acid-rich oils and tends to contain an equimolar mixture of the 9c,11t- and 10t,12c-isomers (6-8). Production of CFAs converted from LNA, EPA and DHA and experimental evaluation of their physiological activities in vitro and in vivo have also been reported (22, 23). Since alkaline hydrolyzed oils contain several CFA isomers, a re-cent concern in the chemical synthesis of CFAs is the separation of specific isomers. It has been reported that lipases from Geotrichum candidum and Candida rugosa selectively esterify the 9c,11t-isomer of CLA, and enzymatic methods utilizing these lipases are effective for separating the 9c,11t-and 10t,12c-CLA isomers (24-26).Other potential methods for CLA production include the isomerization of linoleic acid using bacteria, such as Lactobacillus plantarum (27, 28). These methods may contribute to the preparation of a CFA fraction with maximal physiological activity.

During the 1980s, it was demonstrated that extracts of grilled ground beef have mutagenesis inhibitory activity and it was subsequently found that the beef-derived antimutagen is CLA (29, 30). The anticarcinogenic activity of CLA has been demonstrated in a chemically induced rat mammary tumor model with an effective range of 0.1-1% in the diet. The inhibitory effects on either the chemical carcinogenesis induced by dimethylbenz(a)anthracene or that by methylnitrosourea, for which the mechanisms of carcinogenesis and tumor progression differ, also indicate that CLA pos-sesses multimodes of antitumor action (31, 32). The inhibitory effects of CLA on the growth of various

human cancer cells including hepatoma, colorectal, breast, and lung have also been studied in vitro (33, 34). Although differences in the 9c,11t-isomer, 10t,12c-isomer and a mixture of isomers have been investigated, it appears that CLA anticancer activity is exerted irrespective of the isomer used (35, 36). Recently, the cytotoxic and anticancer effects of other non-linoleic fatty acids with conjugated double bonds have been examined. There is in vivo research indicating that dietary CLN inhibits azoxymethane-induced colonic aberrant crypt foci in rats (18). There are also several reports indicating the cytotoxic effects of CLN on various human cancer cell lines suggesting that conjugated trienes are stronger anticarcinogens than conjugated dienes (17, 22). In a recent study, the effects of CEPA andCDHA with conjugated triene structure, produced from EPAand DHA by alkaline isomerization, on tumor cells were in-vestigated (23). The cytotoxic actions of CEPA and CDHA were demonstrated in several cancer cell lines including colorectal, hepatoma, lung, breast, and stomach. Although the mechanisms underlying the anticancer effect of CFAs have not yet been fully elucidated, the involvement of the induction of apoptosis, cytokine modulation and inhibition of cancer cell proliferation is demonstrated in vitro and in vivo studies (37, 38).

There are limited reports on the effect of CFA intake on cancer development in humans. It has been reported that an inverse relationship between milk consumption and breast cancer risk in women suggests the anticarcinogenic effect of CLA in milk (39). In another study, breast adipose tissue CLA content in 360 patients who had localized breast cancer (n = 261, cases) and those treated for a benign breast tu-mor (n= 99, controls) was investigated (40). As a result, the CLA content was higher in the breast adipose tissues from controls than that from cases. Recently, it has also been re-ported that in postmenopausal Finnish women, dietary CLA intake and serum CLA level are significantly lower in can-cer patients than incontrols (41). Although direct evidence has not been sufficiently established, these findings suggest that CLA supplementation might be effective for the prevention of breast cancer in humans.

Antiobese and Hypolipidemic Properties of CFAs

Although the fat lowering action of CLA was already re-ported in 1971, this effect has again received attention following a report in 1997 indicating that a supplementation of 0.5% CLA in the diet reduced 60% body fat coupled with a 14% increase in lean body mass in mice(42-44). At present, there are a number of studies demonstrating the antiobese and hypolipidemic effects of CLA in animals including mice, rats and pigs (45-47). We also reported that dietary supplementation of 1% CLA reduces the amount of abdominal white adipose tissue, serum triglyceride (TG) level and liver TG level compared with a control diet in obese model Otsuka Long-Evans Tokushima fatty (OLETF) rats (Fig. 2) (48-51). These effects were attributed to the enhanced fatty acid beta-oxidation and the suppression of fatty acid synthesis in the liver. In addition, CLA enhances fatty acid beta-oxidation even in brown adipose tissue and muscle and enhances oxygen consumption and energy ex-penditure in OLETF rats (52, 53). Growing evidence indicates that individual isomers of CLA have specific physiological functions in lipid metabolism. We have reported that the 10t,12c-CLA isomer reduces the secretion of apolipoproteinB100 in cultured human hepatoma HepG2 cells and exerts its hypolipidemic effect by promoting energy metabolism in OLETF rats (53, 54). The body-fat-lowering effect of CLA has also been reported in humans, but it seems to be less prominent than that in rodents. A small-scale randomized clinical trial conducted in Norway was the first to investigate the effect of CLA on body fat in humans. Healthy and physically active men and women took either a CLA mixture (1.8 g/d) or olive oil for 3 months (55). By the end of trial, subjects taking CLA supplements had a 4% decrease in body fat content. The other study from the same group was conducted to examine the dose-response relationship between CLA and body fat mass in obese and overweight subjects (56). In the study, the authors concluded that a dietary supplementation of CLA at 3.4 g/d was sufficient for body fat reduction in obese and overweight subjects over a 3-month period.

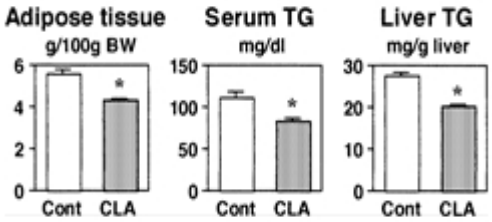

Fig. 2. Antiobese and hypolipidemic effects of CLA in OLETF rats. Asterisk shows significant Difference at P < 0.05.

The antiobese effects of other non-linoleic fatty acids with conjugated double bonds have also been reported. A dietary supplementation of CLN, produced by alkaline isomerization of LNA, reduced body fat content by enhancing of fatty acid beta-oxidation in rats (57). Antiobese and hypolipidemic effects of CLN were also reported in studies with chickens, obese rats and human liver-derived cells (58-60).As new approaches concerning antiobese treatment, the combined effects of CFA and other dietary components are now being evaluated. It has been reported that the body-fat-reducing potential of CLA could be enhanced by a combi-nation with soybean protein and sesamin (61, 62). In a fu-ture study, multiple combinations of various food factors

Newly Identified Bioactivities of CFAs

Many claims for health benefits other than anticancer and antiobesity effects have been made for CLA in animal studies. Antiatherogenic effects of CLA have been reported instudies with rabbits and hamsters. Feeding 0.5 g of CLA/d for 22 weeks and a 1%-CLA-supplemented diet for 12weeks are sufficient in reducing aortic fatty streak area in rabbits and hamsters, respectively (63, 64). The antidiabetic effects of CLA have been reported in studies with obese, diabetic rats. In the first study, feeding of a 1.5% CLA diet normalized impaired glucose tolerance, and the effect of CLA was similar to that of the pharmaceutical agent troglitazone (65). In a subsequent study, it was suggested that the antidiabetic effects of CLA are attributable to the specific action of the 10t,12c-isomer (66). CLA has also shown effects on immune functions. In rats, splenic levels of im-munoglobulin A (IgA), IgG and IgM increase while those of IgE decrease significantly in animals fed the 1.0% CLA diet (67). In another study, a significant increase in the IgA, IgG and IgM productivities of rat spleen lymphocytes was rec-ognized at 0.05% CLA supplementation (68). Very recently, the hypotensive poperties of CLA have also been observed in our studies. In obese, diabetic Zucker rats and obese OLETF rats, the feeding of a CLA mixture and the 10t,12c-CLA isomer prevented the development of obesity-induced hypertension (Fig. 3) (69, 70). We also reported that dietary CLA prevents the development of essential hypertension innonobese spontaneously hypertensive rats (71). These effects were attributable to the ability of CLA to regulate the pro-duction of physiologically active adipocytokines, such as adiponectin, leptin and angiotensinogen (Fig. 4).Considering the previous studies indicating that conjugated trienoic fatty acids have stronger cytotoxic activities than conjugated dienoic fatty acids, the evaluation of the physiological bioactivities of CFA isomers other than CLA on atherosclelosis, diabetes, allergy and hypertension will be of great interest in future studies.

References

1. Nagao, T., Shimada, Y., Yamauchi-Sato, Y., Yamamoto, T.,Kasai, M., Tsutsumi, K., Sugihara, A., and Tominaga, Y.:Fractionation and enrichment of CLA isomers by selectiveesterification with Candida rugosa lipase. J. Am. Oil Chem.Soc., 79, 303-308 (2002).
2. Nagao, T., Yamauchi-Sato, Y., Sugihara, A., Iwata, T.,Nagao, K., Yanagita, T., Adachi, S., and Shimada, Y.: Purification of conjugated linoleic acid isomers through a process including lipase-catalyzed selective esterification. Biosci.Biotechnol. Biochem., 67, 1429-1433 (2003).
3. Kishino, S., Ogawa, J., Ando, A., Omura, Y., and Shimizu,S.: Ricinoleic acid and castor oil as substrates for conjugated linoleic acid production by washed cells of Lactobacillus plantarum. Biosci. Biotechnol. Biochem., 66, 2283-2286 (2002).
4. Kishino, S., Ogawa, J., Ando, A., Iwashita, T., Fujita, T.,Kawashima, H., and Shimizu, S.: Structural analysis of con jugated linoleic acid produced by Lactobacillus plantarum,and factors affecting isomer production. Biosci. Biotechnol.Biochem., 67, 179-182 (2003).
5. Y., Cha, J. Y., and Yanagita, T.: Conjugated linoleic acid reduces hepatic microsomal triacylglycerol transfer protein activity and hepatic triacylglycerol mass in obese rats. J. OleoSci., 52,129-134 (2003).
6. Rahman, S. M., Wang, Y. M., Yotsumoto, H., Cha, J. Y.,Inoue, S., and Yanagita, T.: Effect of conjugated linoleicacid on serum leptin concentrations, body fat accumulation and beta-oxidation of fatty acid in OLETF Rats. Nutrition, 17,385-390 (2001).
7. Nagao, K., Wang, Y. M., Inoue, N., Han, S. Y., Buang, Y.,Noda, T., Koda, N., Okamatsu, H., and Yanagita, T.: The 10trans,12cis isomer of conjugated linoleic acid promotes energy metabolism in OLETF rats. Nutrition, 19, 652-656(2003).
8. Yotsumoto, H., Hara, E., Naka, S., Adlof, R. O., Emken,E. A., and Yanagita, T.: 10trans,12cis-linoleic acid reducesapoB secretion in HepG2 cells. Food Res. Int., 31, 403-409(1999).
9. Thom, E., Wadstein, J., and Gudmundsen,O.:Conjugated linoleic acid reduces body fat in healthy exercising humans. J.Int. Med. Res., 29, 392-396 (2001).