



# Bioavailability and Functionality of Conjugated Fatty Acids in Foods

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## Abstract

Dietary conjugated fatty acids are associated with heart disease, obesity, diabetes, cancer and others; in addition, many functions of cell membranes are dependent on lipid composition and lipids ingested through the diet can modify this composition and their biochemical activity. Due to the discoveries of their chemical and physiological properties, there is a growing interest in conjugated fatty acids as well as in the properties of their isomers. Conjugated fatty acids (CFAs) are the general term to describe the positional and geometric isomers of polyunsaturated fatty acids with conjugated double bonds, which are separated by a single carbon-carbon bond rather than being separated by a methylene group (CH<sub>2</sub>). Theoretically, several isomers of conjugated fatty acids are possible, with multiple combinations of numerical, positional and geometric configurations of the conjugation of double bonds, which may present as conjugated linoleic and  $\alpha$ -linolenic acids and may have different functionalities in the body.

**Keywords:** Polyphenols; Conjugated Fatty Acids; Lipid Metabolism; Antioxidant; Inflammation; Punicic Acid; Eleostearic Acid

**Abbreviations:** PSA: Punicic Acid; BSA:  $\alpha$  Eleostearic Acid; SOS: Superoxide Dismutase; GSH: Glutathione Reductase; GPx Glutathione Peroxidase; H<sub>2</sub>O<sub>2</sub>: Hydrogen Peroxide; DPPH: 2,2-Diphenyl-1-picryl-hydrazyl-Hydrate; ORAC: Oxygen Radical Absorbance Capacity; LOX: Lipoxidase; COX: Cyclooxygenase; ROS: Reactive Oxygen Species.

## Introduction

There are a large number of studies in the literature that demonstrate that different fatty acids have a beneficial effects on health through studies using in vivo and in vitro models and can be used to treat acute and chronic conditions, such as ischemia/reperfusion, neurodegeneration, diabetes, cancer and obesity lesions. Among them are the

conjugated fatty acids. Part of these effects observed in the conjugated compounds of fatty acids can be attributed to their antioxidant, anti-inflammatory and anti-proliferative properties [1].

The antioxidant activity of conjugated fatty acids is due to the oxide-reduction potential of their molecules to compete for active sites and receptors in different cellular structures or to participate in the modulation of the genes expression that related to encode proteins involved in intracellular mechanisms in a similar way to phenolic compounds acting in defense of oxidative and degenerative processes of cellular structures. Being able to inhibit the pathway of araquidonic fatty acid metabolism by inhibiting the synthesis of LOX, COX and modifying the cytokines functions [2].

## Fatty Acids and Diet

The physical, chemical and metabolic characteristics of fatty acids provided through the diet are associated with heart diseases, obesity, diabetes, cancer, among others, many functions of cell membranes are dependent on lipid composition and lipids ingested through diet can modify their composition and also modify their biochemical activity [3].

Conjugated fatty acids have been attributed several functions in metabolic processes, especially antioxidant activity that is closely related to the decrease of reactive oxygen species (ROS) and also by the reduction of the lipid peroxidation process [4].

## Conjugated Fatty Acids

Conjugated fatty acids (CFAs) are the general term to describe the positional and geometric isomers of polyunsaturated fatty acids with conjugated double bonds, which are separated by a single carbon-carbon bond rather than being separated by a methylene group (CH<sub>2</sub>). Theoretically, several isomers of AGCs are possible, with multiple combinations of numerical, positional and geometric configurations of the conjugation of double bonds, which can present themselves as conjugated linoleic and  $\alpha$ -linolenic acids [5].

## Conjugated Linoleic Fatty Acids (CLAs)

The conjugated linoleic fatty acids, also called CLAs refer to a group of geometric and positional isomers of octadecadienoic acid that contain double bonds in a conjugated position and may have cis or trans configurations. There are a large number of isomers of CLAs reported. However, due to their biological functions, two main isomers have been the focus of current research: 9cis, 11trans and 10trans, 12cis [6]. The 9c, 11t is the predominant isomer found in natural sources such as meat, milk and dairy products from ruminant animals. This isomer originates from the biohydrogenation of linoleic acid to stearic acid by ruminant bacteria or from the desaturation ( $\Delta 9$ ) of vaccenic acid (C18:1,11t) in the breast tissue. The other major isomer of CLA (10t, 12c) is present in very low concentrations in foods, but is primarily derived from synthetic preparations of CLAs. Most studies with CLAs have used a mixture of these two isomers [7,8].

There are many studies that evaluate the various beneficial effects of CLAs in the body, especially in some experimental animal models. However, the results are controversial and sometimes show some adverse effects such as increased liver lipids [5].

## Linolenic conjugated fatty acids (CLNAs)

The  $\alpha$ -linolenic conjugated fatty acids AGCs, also called CLNAs, short form for conjugated linolenic acids, refer to a group of geometric and positional isomers of octadecatrienoic acid that contain three conjugated double bonds [9]. They are found exclusively in several types of vegetable seed oils, being present in high amounts (40 to 80% of the total fatty acids). Each seed has only one conjugase enzyme that converts linoleic acid into a specific isomer of CLNAs [5].

Research has shown that these isomers of CLNAs are associated with anti-carcinogenic, anti-adipogenic, antioxidant, anti-inflammatory and anti-atherosclerotic properties, both in vitro and in vivo, and their efficacy can vary substantially between individual isomers as well as doses and doses in model used [10,11]. Thus, the conjugation process can result in the production of a series of fatty acids with diverse biogenic profiles.

Compared to CLAs, studies on the physiological effects of CLNAs are even more limited [11]. However, studies have shown that these isomers are well absorbed by the body, being metabolized and incorporated in the form of CLAs in animal tissues. Therefore, some biological effects of CLNAs can be partially explained by being attributed to CLAs [12].

However, the difference in the configuration of the double bond at carbon 13 cis or trans of these two isomers, confer differences in the rate of metabolism and in the intensity and biological activities [5,12].

## Studies of Conjugated Fatty Acids at FBA-FCF-University of Sao Paulo

Studies carried out at the Lipid Laboratory of the Food and Experimental Nutrition Department at FCF/USP confirmed the presence in high percentages of puniceic (57%) and  $\alpha$ -eleostearic (24%) fatty acids in relation to the total lipids present in pomegranate and bitter gourd seeds, respectively [5,13,14]. Furthermore, in vitro antioxidant activities of these oils were demonstrated by different methods (beta-carotene/linoleic acid system, DPPH radical scavenging, ORAC). Another interesting result was that, in rats fed for 40 days with these oils, more 9c,11t-CLA were found than CLNAs itself in tissue lipids, but in a discriminated way and with different intensities in each tissue studied, CLAs being found mainly in adipose and liver tissue.

The fatty acid profile of the liver is a determining factor in the presence of diseases such as hepatic steatosis and inflammation [15]. However, there is no consensus in the literature regarding the effects of the 9c, 11t-CLA isomer (metabolite resulting from CLNAs) on lipid metabolism, as

well as the absence of studies in this regard related to CLNAs. In this sense, the biological impact and mechanisms of action of these fatty acids (CLAs and CLNAs) must be considered, since they could interfere with lipid metabolism and exert other health effects, acting as an antioxidant and anti-inflammatory [4].

The determination of oxidative stress in liver cells induced by the presence of fatty acids uses not only the activity of SOD, but also the levels of GSH; whose data are results inversely related to the levels of reactive species [16]. Briefly, in normal cells, SOD plays a fundamental role under peroxides, which can still be neutralized by CAT or GPx. The GPx neutralizes hydrogen peroxide using GSH as a substrate [17]. Thus, collectively, enzymes can play the role of antioxidant defense with the participation of the stimulus of conjugated fatty acids found in the oils of pomegranate and bitter melon seeds.

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