Review

Biotechnological production of conjugated linoleic acid

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Abstract: Although the term "conjugated linoleic acid (CLA)" involves 56 isomers of linoleic acid (LA), only two of them (c9,t11-CLA and t10,c12-CLA) have exhibited positive effects to human body. A great demand for preferred conjugated isomers of LA motivates researchers to look for the possible biotechnological methods of their preparation instead of chemical synthesis. This leads to a mixture of various unexpected CLA isomers that have to be further separated. Since past decade, several microbial species (*Lactobacillus*, *Propionibacterium*, *Bifidobacterium*, rumen bacteria) and biotechnological techniques have been studied with the aim to transform a range of substrates into desired CLA metabolites. This review describes various microorganisms and different methods that have been employed for microbial CLA formation.

Key words: conjugated linoleic acid, bacteria, biotechnology.

Abbreviations: CLA, conjugated linoleic acid; LA, linoleic acid; SO, polyoxyethylene sorbitan monooleate.

Introduction

Conjugated linoleic acid (CLA) is a generic name for a mixture of positional and geometric isomers of linoleic acid (LA, 9c,12c-octadecadienoic acid, C18:2) with conjugated double bonds at 7 and 9, 8 and 10, 9 and 11, 10 and 12, 11 and 13 or 12 and 14 positions. This fatty acid arises along a stepped pathway carried out by rumen bacteria in the ruminal process which ends with full saturation of LA into stearic acid. These naturally occurring groups of dienoic derivatives of LA are incorporated into the fat in beef and milk of ruminants before the saturation process has been completed. Food products from ruminants, particularly dairy products, are the major dietary source of CLA for humans (Khanai & Dhiman, 2004).

Research on CLA isomers was initiated in the 1930s, when the fact that they absorb UV light at $\geq$ 230 nm was discovered (Miller & Burr, 1937). Because natural body fat absorbs very little at these wavelengths, it was possible to use conjugated fats as markers of lipid metabolism. Between 1938 and 1958 research was carried out to describe their biological activity. Interest in CLA isomers increased in the 1980s when their potent anticancer effects were first reported (Pariza & Hargraves, 1985). Over the last 20 years biological activities of particular CLA isomers have been studied intensively.

Of the various CLA isomers, the cis-9, trans-11 and the trans-10, cis-12 (c9,t11 and t10,c12, respectively) configurations are considered to be the most effective (Fig. 1). They have attracted attention because of their potential health benefits, such as anticarcinogenic, antiadipogenic, antiatherogenic, and antidiabetic effects (Pariza, 1999; Banni et al., 2003; Belury, 2003; Kritchevsky, 2003). CLA roles in vitamin A metabolism (Carta et al., 2002), bone modeling (Watkins et al., 2003), platelet aggregation (Truitt et al., 1999) and immune response (Cook et al., 2003) have also been reported. Other novel applications of CLA are oriented towards foods, skin care products and cosmetics (Kapoor et al., 2003). Some of the biological activity of the two major CLA isomers may result from their different involvement in fatty acid metabolism (Bretillon et al., 1999).

Great interest in CLA effects has lead to looking for the suitable way for CLA production. Nowadays, the most CLA is synthesized chemically and is sold as food supplement. However, a disadvantage of chemical preparation of CLA is a mixture of various unexpected isomers. Considering the use of CLA for nutraceutical purposes, effort is focused on production of only desired CLA compounds. From this point of view, the biotechnological techniques are interesting alternatives due to the ability of microorganisms to biosynthesize desired CLA metabolites. The introduction of biological reactions to CLA production may thus solve the problem of by-production of unwanted CLA isomers. Moreover,

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