Plant stanol and stanol ester: comparison on mimicking property for LDL lowering purpose

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Abstract

Hyperlipoproteinemia is classified as an important risk for cardiovascular disease. At present, the standard treatment is with statins. However, statins may have some unfavorable side effects. Recently, a new concept, namely the use the plant derived stanol for lowering of LDL level was proposed. The author has performed an analysis on the structure of plant stanol compared to plant stanol ester, with the aim of assessing its efficacy in mimicking LDL. It can be seen that the plant stanol ester has less difference in size comparing to LDL. This implies the better mimicking effect of plant stanol ester than plant stanol.

Key words: plant, stanol, stanol ester

Introduction

The relationship between Lipoprotein disorders and atherosclerosis has been well documented for several years. In addition, the relationship with clinical manifestations including myocardial infarction, stroke, and sudden cardiac death, has been conclusively demonstrated. The reduction of low density lipoprotein (LDL) cholesterol is accepted for its importance in the prevention of coronary heart disease and other atherosclerotic diseases. The medical management of hypercholesterolemia has been studied in many clinical trials. At present, the standard treatment with statins has been effective in decreased cardiovascular morbidity and global mortality. However, some unfavorable side effects of statin have been noted.

Recently, a new concept, the use the plant derived stanol for lowering of LDL levels was proposed by a study group in Finland. The main theory is based on the mimicking effect of plant stanol that results in the reduction of LDL. At present, two main forms of plant statinol, stanol (sterol) and stanol ester, have been launched for use. The main difference between the two forms is that stanol is not saturated but stanol ester is. The effectiveness of the two products has been mentioned in published literature. However, there is no systematic analysis to compare the efficacy of the two products. The author has performed an analysis on the structure of plant stanol compared to stanol ester aimed at assessing of its efficacy in mimicking LDL.
Materials and methods

Structural analysis of the plant stanol and stanol ester

This was performed as a bioinformatics experimental study by Geometrical analysis of plant stanol and stanol ester is performed using the Swiss-Pdb Viewer application that allows the analysis of several proteins at the same time. (GlaxoSmithKline R&D & the Swiss Institute of Bioinformatics). This technique is already described and proved for reliability in the previous published work.

Comparison to the structure of LDL

The comparison to the structure of LDL is further done based on the principle of chemoinformatics. Based on the primary assumption that the chemical property of plant stanol in both forms can effectively mimic LDL, the main comparison in this study is the size comparison.

Results

According to the geometrical analysis, the average size of plant stanol and stanol ester is about 11 nm and 23 nm. The standard LDL has its average size about 25 nm. The difference in size in case of plant stanol and plant stanol ester are about 14 nm and 2 nm.

Discussion

Hyperlipoproteinemia is classified as an important risk for cardiovascular disease. The use of plant stanol for LDL reduction is the new alternative modality for management of high serum LDL level. Many clinical trials have proven that plant sterol and stanol esters can effectively decrease high serum total and LDL cholesterol. They reduce the intestinal absorption of cholesterol by decreasing the incorporation of dietary and biliary cholesterol into micelles displacing cholesterol from these micelles. They also increase LDL receptor activity on liver cells causing a higher uptake of LDL cholesterol and thus decreasing the serum LDL cholesterol concentration. In trials, it has been detected that the plant stanol, either stanol or stanol ester could significantly reduce the blood lipid within 1 – 2 months without reported adverse effect. Hence, these are accepted as food additive ingredients. Also, it is reported that adding plant stanol to the standard statin treatment can increased lipid lowering action. In the long term follow up, use of plant stanol combined with simvastatin treatment can reduce cholesterol absorption and serum cholesterol more consistently in subjects with high than low baseline absorption of cholesterol, implying the main mechanism of plant stanol, disturbance of cholesterol absorption.

Basically, the plant stanol bind the micelle with higher affinity than LDL and this is called mimicry phenomenon. This results in reduction of serum LDL. The stanol ester is a larger molecule containing the esterified part and this leads to the nature of saturated particles. However, both substances are comparatively absorbed with cholesterol. In general, the two forms, plain form and ester form, of plant stanol are in use. The effectiveness of both forms is mentioned. Although the LDL-lowering effect of plant sterol ester is less marked in longer-term than in short-term usages the plant stanol ester still maintains the efficacy at satisfactory level. Hence, there should be and must be some difference owing to the fact that both are not the same chemical substance.
Here, the author analyzes the structure of plant stanol and stanol ester using standard bioinformatic techniques. It can be seen that the plant stanol ester has less difference in size comparing to LDL. This implies the better mimicking effect of plant stanol ester than plant stanol. This supports the recent publication that unesterified plant stanols might not affect LDL electrophoretic characteristics in hypercholesterolemic subjects\textsuperscript{12}. Also, it is in concord with the suggestion of O’Neill et al that plant stanol ester was preferable for long term control of hyperlipoproteinemia\textsuperscript{7}. As a conclusion, based on the result in this work, the difference observed in LDL lowering between stanol and stanol ester is mainly due to difference in tertiary structure rather than due to the change in electric charge of the molecule that affects the binding site or due to the altered clearance of the esters. Indeed, the fact that the mechanism of working of the two substances in clearing of the LDL is not different and the cited study on no change in electrophoretic characteristic\textsuperscript{12} supports this conclusion.

References