Cholesterol-lowering efficacy of *Lactobacillus plantarum* CECT 7527, 7528 and 7529 in hypercholesterolaemic adults

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Abstract

Previous studies have indicated that supplementation with probiotic bacteria may improve lipid metabolism. The present study was aimed at investigating the effects of a mixture of three strains of *Lactobacillus plantarum* (CECT 7527, CECT 7528 and CECT 7529) on cholesterol-lowering efficacy in hypercholesterolaemic patients. A total of sixty volunteers (thirty participants in the placebo group and thirty counterparts in the *L. plantarum* group), aged 18–65 years old, participated in a controlled, randomised, double-blind trial. The study group received one capsule daily containing 1.2×10⁹ colony-forming units of *Lactobacillus* strains in a unique dose; the placebo group consumed the same product without bacteria for 12 weeks. A significant reduction of 13.6% in plasma total cholesterol (TC) levels was observed after 12 weeks of consumption in the *L. plantarum* group when compared with the placebo group. The lipidic outcomes were also analysed based on TC values at baseline: low initial values (LIV, 2000–2500 mg/l) v. high initial values (HIV, 2510–3000 mg/l). In the HIV group, the *L. plantarum* treatment showed a reduction after 12 weeks of consumption compared with the placebo group in TC, LDL-cholesterol (LDL-C) and oxidised LDL-C (17.4, 17.6 and 15.6%, respectively). In the LIV, the *L. plantarum* treatment only showed a reduction after 12 weeks of consumption when compared with the placebo group in TC (9.4%). The present results showed that the biofunctionality of *L. plantarum* (CECT 7527, CECT 7528 and CECT 7529) is proportional to the cardiovascular risk of the patient, having a better effect in patients with higher levels of cholesterol.

Key words: Probiotic bacteria: *Lactobacillus plantarum*: LDL-cholesterol: CVD

CVD remain the biggest cause of deaths worldwide. More than seventeen million people died from CVD in 2008. More than three million of these deaths occurred before the age of 60 years and could have largely been prevented¹. Raised blood cholesterol increases the risk of heart disease and stroke². Globally, one-third of IHD is attributable to high cholesterol³. Moreover, it has been shown that a 1% reduction in serum cholesterol is associated with an estimated reduction of 2–3% in the risk of coronary artery disease⁴. There are different pharmacological agents that are available to treat this condition (e.g. statins or bile acid sequestrants); however, they are often suboptimal and expensive and can have unwanted side effects⁵. There is an increasing interest in non-drug therapies to improve the blood cholesterol profile, particularly when drug treatment is considered unsuitable due to elevated cost, safety reasons or just personal preference. Dietary recommendations and exercise are the first line of therapy for individuals with elevated cholesterol values; however, using these methods, only a modest amelioration can be achieved⁶. Probiotics, in general, are defined as ‘live microorganisms that, when administered in adequate amounts, confer a health benefit on the host’⁷. They are regarded as safe for human consumption and numerous (functional) food and nutraceutical products are available in the marketplace⁸,⁹. In the last years, efforts have been underway to develop probiotics that can help to reduce blood cholesterol and the risk of CVD¹⁰–¹³.

Strains of lactic acid bacteria were isolated from the faeces of healthy infants as described in Bosch et al.¹⁴. Extensive *in vitro* characterisation of 550 of these strains was carried out to look for candidate strains with the capacity to deconjugate bile acids, to assimilate cholesterol and to produce SCFA, which can then cause a decrease in the systemic levels of blood lipids. *Lactobacillus plantarum* CECT 7527, CECT 7528 and CECT 7529 were selected among the 550 strains for its individual capacity in performing the functionalities

Abbreviations: HDL-C, HDL-cholesterol; HIV, high initial value; LDL-C, LDL-cholesterol; LIV, low initial value; OX-LDL, oxidised LDL-cholesterol; TC, total cholesterol.

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Probiotic strains for reducing cholesterol

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Each participant consumed the probiotic treatment composed of a mixture of three strains in the same proportion of *L. plantarum* (CECT 7527, 7528 and 7529, AB-LIFE): 1 · 2 × 10^9 colony-forming units daily dose, or the control product without bacteria. They were adequately stored before use and therefore the level of lactobacilli was constant throughout the shelf-life of the product. The study consisted of two phases: a treatment period (12 weeks) and a washout period (4 weeks). The study included a baseline visit of selection, a visit at the midpoint and endpoint of the treatment period (weeks 6 and 12, respectively), and a fourth visit after the washout period (week 16).

**Blood sampling and biochemical measurements**

Blood for assessment of the lipid profile was collected at each visit. Following an overnight fast (12 h), a blood sample was obtained from each participant. Serum samples were analysed enzymatically for TC, LDL-C, oxidised LDL-cholesterol (OX-LDL), HDL-cholesterol (HDLC) and TAG. Blood for the assessment of the safety profile was collected at the beginning and end of the study. Serum biochemistry was analysed for creatinine, aspartate transaminase, alanine transaminase and γ-glutamyl transpeptidase. Serum analysis was performed on a Dimension RxL biochemistry analyser using appropriate reagent kits (Dade Behring, Siemens).

**Statistical analysis**

Study data were treated in accordance with the established norms of confidentiality and quality criteria described in the protocol. Statistical analysis of the data was done using SPSS for Windows version 18 software (PASW Statistics; IBM Corporation). Descriptive presentation of the data was performed through means as the measure of the trend of endpoint values measured in the study. To this end, mean values of each studied parameter across time of each experimental day were determined. A comparative analysis of the values obtained throughout the study period was performed. Data are presented as means with their standard errors. The variations in the parameters throughout time for each of the treatments were analysed by the general linear model for repeated measures, both at intra- and inter-group levels, considering the visit as the intra-group factor and treatment as the inter-group factor. Differences in the dietary intake of macronutrients were analysed using a one-way ANOVA. The data of the stratification of the patients (which were not included initially in the protocol) were analysed using 95% CI. In all hypothesis tests, the null hypothesis of equality between means was rejected when the *P* value was lower than 0·05, which means that significant differences were considered when *α* or type I error were < 0·05.

**Results**

**Baseline characteristics of subjects**

The baseline characteristics for the sixty subjects (anthropometric characteristics, values of safety and efficacy variables) mentioned above. The combination of the three strains in mixed cultures produced better results in the different functionalities studied than the individual strains (M Bosch, MC Fuentes, S Audirvent, MA Bonachera, S Peiró and J Cuné; unpublished results). It has been hypothesised that deconjugation of bile acids leads to a reduction in serum cholesterol by increasing cholesterol catabolism during the formation of new bile acids\(^{15}\). Thus, the aim of the present study is to perform a controlled evaluation of the effects of AB-LIFE\(^{1,2}\), a probiotic formula with three different strains of *L. plantarum* (CECT 7527, CECT 7528 and CECT 7529), on the concentration of lipids and other parameters related to cardiovascular risk in hypercholesterolaemic subjects.

**Experimental methods**

**Participants**

The present study was carried out according to the Declaration of Helsinki and written informed consent was obtained from all subjects. The protocol was approved by the Ethical Committee of the Hospital Universitario Puerta de Hierro, Madrid, Spain (protocol 106/2009).

A total of sixty subjects were randomly distributed into two groups: placebo or *L. plantarum*. No patient dropped out of the study. Subjects were eligible for the study if male or female (non-pregnant), aged 18–65 years, with total cholesterol (TC) between 2000 and 3000 mg/l (5·16 and 7·64 mmol/l), BMI between 19 and 30 kg/m² and LDL-cholesterol (LDL-C) values between 1300 and 1900 mg/l (3·35 and 4·91 mmol/l). Subjects were not included in the case of plasma TAG levels ≥ 3500 mg/l (≥ 3·85 mmol/l), a previous cardiovascular event within the last 6 months, the presence of secondary dyslipaemias related to thyroid dysfunction or the use of any drug affecting lipid metabolism.

**Study design**

A single-centre, prospective, randomised, double-blind, placebo-controlled, parallel-group trial was designed. According to the suggestion made by the ethical committee, lifestyle recommendations were given to the participants during the baseline visit of selection (Estrategia Naos, Spanish strategy for nutrition, physical activity and the prevention of obesity); however, they did not receive a specific diet or were institutionalised. The participants agreed to take the product as a dietary supplement and to not change dramatically their regular diets or physical activity in order to study the effect of the supplement in a conventional hypercholesterolaemic lifestyle. As dietary recommendations were given to the patients, to study whether there were some important changes from their conventional diet, dietary intake, including information about total energy, percentage of total fat, percentage of total carbohydrates and percentage of total protein of both groups, was measured at baseline and endpoint (week 12) of the treatment period. On the day of the baseline and endpoint visits, nutritional anamnesis of the participants was collected from the 7 d previous to the visit.
were compared in the placebo and *L. plantarum* groups. The two groups produced by randomisation were homogeneous in terms of anthropometric and clinical characteristics (Table 1). Subjects were selected based on fasting serum TC (2000–3000 mg/l) and LDL-C (1300–1900 mg/l). The mean serum concentrations of TC and LDL-C at baseline were not significantly different between the placebo and treatment groups (2526 ± 2474 and 1683 ± 1666 mg/l, respectively).

### Dietary intake

An analysis of total energy, percentage of total lipids, percentage of total carbohydrates and percentage of total proteins of both groups was performed at baseline and endpoint (week 12) of the treatment period (Table 2). There were no significant differences between the placebo and *L. plantarum* groups at baseline or endpoint. Moreover, there were no significant differences between the treatments in relation to weight, BMI, fat-free fat mass and fat mass after 12 weeks of consumption of the probiotic (placebo: 74·9 (SEM 2·1) kg; 25·9 (SEM 0·4) kg/m²; 58·1 (SEM 1·7) kg; 16·8 (SEM 0·7) kg and *L. plantarum*: 73·9 (SEM 2·1) kg; 25·5 (SEM 0·4) kg/m²; 57·1 (SEM 1·7) kg; 16·8 (SEM 0·7) kg).

### Serum lipid profile

**Global data.** The changes in TC, LDL-C, HDL-C, LDL-C: HDL-C, OX-LDL and TAG during the treatment period and after 4 weeks of the washout period are summarised in Table 3. After 6 weeks of consumption, no significant differences were detected in lipid profile variables between the treatments at baseline and at the end of the treatment period (week 12) (Table 1).

**Table 1.** Comparison of anthropometric, safety and efficacy variables in the placebo and *Lactobacillus plantarum* treatments at baseline (Mean values with their standard errors)

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n 30)</th>
<th>L. plantarum (n 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SEM</td>
</tr>
<tr>
<td><strong>Body weight (kg)</strong></td>
<td>75·1 ± 2·02</td>
<td>74·8 ± 2·26</td>
</tr>
<tr>
<td><strong>Height (cm)</strong></td>
<td>169·8 ± 1·64</td>
<td>169·6 ± 1·84</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>26·0 ± 0·44</td>
<td>25·9 ± 0·45</td>
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<tr>
<td><strong>FFM (kg)</strong></td>
<td>58·1 ± 1·59</td>
<td>57·7 ± 1·73</td>
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<tr>
<td><strong>FM (kg)</strong></td>
<td>17·0 ± 0·69</td>
<td>17·1 ± 0·69</td>
</tr>
<tr>
<td><strong>Systolic BP (mmHg)</strong></td>
<td>115·8 ± 2·75</td>
<td>114·4 ± 2·87</td>
</tr>
<tr>
<td><strong>Diastolic BP (mmHg)</strong></td>
<td>71·9 ± 1·82</td>
<td>71·0 ± 1·53</td>
</tr>
<tr>
<td><strong>Pulse (bpm)</strong></td>
<td>76·7 ± 1·74</td>
<td>74·3 ± 1·55</td>
</tr>
<tr>
<td><strong>Creatinine (mg/l)</strong></td>
<td>8·4 ± 0·2</td>
<td>8·3 ± 0·2</td>
</tr>
<tr>
<td><strong>AST (UI/l)</strong></td>
<td>16·4 ± 1·04</td>
<td>17·4 ± 1·04</td>
</tr>
<tr>
<td><strong>ALT (UI/l)</strong></td>
<td>16·5 ± 1·13</td>
<td>16·7 ± 1·13</td>
</tr>
<tr>
<td><strong>GGT (UI/l)</strong></td>
<td>18·7 ± 1·29</td>
<td>19·5 ± 1·29</td>
</tr>
<tr>
<td><strong>TC (mg/l)</strong></td>
<td>2526 ± 42·9</td>
<td>2474 ± 57·1</td>
</tr>
<tr>
<td><strong>LDL-C (mg/l)</strong></td>
<td>1683 ± 35·9</td>
<td>1666 ± 39·5</td>
</tr>
<tr>
<td><strong>HDL-C (mg/l)</strong></td>
<td>463 ± 18·7</td>
<td>442 ± 12·6</td>
</tr>
<tr>
<td><strong>LDL-C:HDL-C ratio</strong></td>
<td>3·82 ± 0·17</td>
<td>3·85 ± 0·14</td>
</tr>
<tr>
<td><strong>OX-LDL (UI/l)</strong></td>
<td>56·4 ± 2·82</td>
<td>54·7 ± 2·01</td>
</tr>
<tr>
<td><strong>TAG (mg/l)</strong></td>
<td>1896 ± 140</td>
<td>1800 ± 134</td>
</tr>
</tbody>
</table>

**Dietary intake.** After 12 weeks of consumption of the probiotic (*L. plantarum*: 73·9 kg/m²; 25·5 kg/m²; 57·1 kg; 16·8 kg) and the placebo (74·9 kg/m²; 25·9 kg/m²; 58·1 kg; 16·8 kg), there were no significant differences between the treatments in relation to weight, BMI, fat-free fat mass and fat mass after 12 weeks of consumption of the probiotic (*L. plantarum*: 73·9 kg/m²; 25·5 kg/m²; 57·1 kg; 16·8 kg) and the placebo (74·9 kg/m²; 25·9 kg/m²; 58·1 kg; 16·8 kg). In relation to HDL-C, although higher than those obtained in the placebo group for TC (2138 v. 2420 mg/l) and LDL-C (1166 mg/l v. 1422 mg/l), the *L. plantarum* group showed a significant increase in HDL-C levels compared with baseline (471 v. 442 mg/l), and this effect was not observed in the placebo group.

**Serum lipid profile.** The lipidic outcomes were also analysed based on TC values at baseline: low initial values (LIV) 2000–2500 mg/l v. high initial values (HIV) 2510–3000 mg/l (Table 4). After 6 weeks of consumption, no significant differences were detected in lipid profile variables between the treatments in any of the groups. In the HIV group, after 12 weeks of treatment, the values obtained after 12 weeks of consumption in the *L. plantarum* group were significantly lower than those obtained in the placebo group for TC (2138 v. 2420 mg/l). In the case of LDL-C and OX-LDL, the *L. plantarum* group after 12 weeks of consumption showed a change in HDL-C levels compared with baseline (471 v. 442 mg/l), and this effect was not observed in the placebo group.

**Stratification of the patients.**
Table 3. Evolution of lipid parameters in the placebo and *Lactobacillus plantarum* treatments after 6 and 12 weeks of consumption and after the washout period (week 16)†

(Mean values with their standard errors)

<table>
<thead>
<tr>
<th></th>
<th>After 6 weeks of consumption</th>
<th>After 12 weeks of consumption</th>
<th>After 4 weeks of washout period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (n 30)</td>
<td><em>L. plantarum</em> (n 30)</td>
<td>Placebo (n 30)</td>
</tr>
<tr>
<td></td>
<td>Mean  SEM</td>
<td>Mean  SEM</td>
<td>Mean  SEM</td>
</tr>
<tr>
<td>TC (mg/l)</td>
<td>239³ B 42·0</td>
<td>2329 b 47·5</td>
<td>NS 2420 C 41·4</td>
</tr>
<tr>
<td>LDL-C (mg/l)</td>
<td>1568³ 33·3</td>
<td>1549 b 34·1</td>
<td>NS 1585 C 33·2</td>
</tr>
<tr>
<td>HDL-C (mg/l)</td>
<td>467³ 18·2</td>
<td>447 a 13·5</td>
<td>NS 467 a 13·4</td>
</tr>
<tr>
<td>LDL-C:HDL-C ratio</td>
<td>3·51-0·16</td>
<td>3·56 b 0·13</td>
<td>NS 3·56 b 0·10</td>
</tr>
<tr>
<td>OX-LDL (U/l)</td>
<td>52-7 1·74</td>
<td>51-4 a 1·86</td>
<td>NS 55-4 c 1·52</td>
</tr>
<tr>
<td>TAG (mg/l)</td>
<td>182-4 137·2</td>
<td>167 b 115·7</td>
<td>NS 184 a 135</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo (n 30)</td>
<td><em>L. plantarum</em> (n 30)</td>
<td>Placebo (n 30)</td>
</tr>
<tr>
<td></td>
<td>Mean  SEM</td>
<td>Mean  SEM</td>
<td>Mean  SEM</td>
</tr>
</tbody>
</table>
| TC, total cholesterol; LDL-C, LDL-cholesterol; HDL-C, HDL-cholesterol; OX-LDL, oxidised LDL-cholesterol.

A,B,C Mean values with unlike superscript upper-case letters were significantly different in the placebo group at the intra-group level (*P*, 0·05).

a,b,c Mean values with unlike superscript lower-case letters were significantly different in the group at the intra-group level (*P*, 0·05).

* P values indicate significant inter-group differences.

† The baseline values are in Table 1.
is likely that in future studies with a higher number of participants, this effect could be observed.

When examining the cholesterol-lowering trend over the course of the study, it is apparent that the time to maximal therapeutic effect may be longer than in other cholesterol-lowering therapies\(^\text{19}\). In the present study, a significant reduction in TC (5.9%) was observed after 6 weeks of consumption in the L. plantarum group when compared with the baseline value. However, there was not a significant effect when compared with the placebo group because a similar reduction in TC, total cholesterol; LDL-C, LDL-cholesterol; HDL-C, HDL-cholesterol; OX-LDL, oxidised LDL-cholesterol.

The maximal therapeutic effect in the Placebo group when compared with the baseline (9.4% and 11.5%, respectively). This finding may favour a major reduction in plasma cholesterol. It is

\[ \text{TC (mg/l)} \quad \text{L. plantarum (n 14)} \]

\[
\begin{array}{cccc}
\text{Placebo} & \text{L. plantarum} & \text{Placebo} & \text{L. plantarum} \\
\text{Baseline} & \text{After 6 weeks of consumption} & \text{Baseline} & \text{After 12 weeks of consumption} \\
\hline
\text{Placebo (n 17)} & \text{L. plantarum (n 14)} & \text{Placebo (n 17)} & \text{L. plantarum (n 14)} \\
\text{Mean} & \text{SEM} & \text{Mean} & \text{SEM} & \text{Mean} & \text{SEM} & \text{Mean} & \text{SEM} \\
\hline
> 2500 mg/l

\text{TC (mg/l)}

2703\(^a\) & 30-3 & 2769\(^a\) & 40-2 & NS & 2550\(^b\) & 37-1 & 255b\(^c\) & 42-4 & NS & 2574\(^a\) & 35-8 & 2286\(^e\) & 40-3 & < 0.05 \\
LDL-C (mg/l) & 1831\(^a\) & 22-3 & 1866\(^a\) & 8-3 & NS & 1699\(^b\) & 25-8 & 171b\(^c\) & 12-3 & NS & 1717\(^a\) & 25-8 & 153a\(^b\) & 14-5 & < 0.05 \\
HDL-C (mg/l) & 458\(^a\) & 20-9 & 448\(^a\) & 14-9 & NS & 461\(^a\) & 20-7 & 451\(^a\) & 17-2 & NS & 461\(^a\) & 21-2 & 479\(^a\) & 17-9 & NS \\
LDL-C:HDL-C ratio & 4-15\(^a\) & 0-19 & 4-23\(^a\) & 0-14 & NS & 3-81\(^a\) & 0-19 & 3-88\(^a\) & 0-15 & NS & 3-85\(^a\) & 0-19 & 3-28\(^a\) & 0-14 & NS \\
OX-LDL (U/l) & 61-5\(^a\) & 1-56 & 63-5\(^a\) & 1-14 & NS & 57-5\(^a\) & 1-51 & 59-5\(^a\) & 1-04 & NS & 60-2\(^a\) & 1-56 & 53-6\(^b\) & 1-14 & < 0.05 \\
TAG (mg/l) & 2054\(^a\) & 173-4 & 223\(^a\) & 198 & NS & 1961\(^a\) & 172-7 & 200\(^a\) & 169 & NS & 2007\(^a\) & 170 & 178\(^a\) & 158 & NS \\
< 2500 mg/l

\text{TC (mg/l)}

2295\(^a\) & 28-2 & 2217\(^a\) & 33-5 & NS & 2189\(^a\) & 36-0 & 2131\(^a\) & 34-7 & NS & 2219\(^a\) & 36-7 & 2008\(^b\) & 24-3 & < 0.05 \\
LDL-C (mg/l) & 1490\(^a\) & 29-2 & 1491\(^a\) & 35-2 & NS & 1397\(^a\) & 26-8 & 1401\(^a\) & 31-2 & NS & 1414\(^a\) & 25-5 & 1319\(^b\) & 21-9 & < 0.10 \\
HDL-C (mg/l) & 472\(^a\) & 34-4 & 438\(^a\) & 20-1 & NS & 475\(^a\) & 33-2 & 444\(^a\) & 20-9 & NS & 475\(^a\) & 32-6 & 464\(^a\) & 20-1 & NS \\
LDL-C:HDL-C ratio & 3-38\(^a\) & 0-27 & 3-52\(^a\) & 0-20 & NS & 3-13\(^a\) & 0-23 & 3-27\(^a\) & 0-18 & NS & 3-18\(^a\) & 0-24 & 2-92\(^a\) & 0-14 & NS \\
OX-LDL (U/l) & 49-8\(^a\) & 2-78 & 47-0\(^a\) & 2-28 & NS & 46-5\(^a\) & 2-69 & 44-3\(^a\) & 2-15 & NS & 49-1\(^a\) & 2-72 & 41-7\(^a\) & 1-73 & NS \\
TAG (mg/l) & 1690\(^a\) & 225-0 & 142\(^a\) & 123 & NS & 1644\(^a\) & 220 & 1387\(^a\) & 119 & NS & 1635\(^a\) & 213 & 126\(^a\) & 116 & NS \\
\end{array}
\]

\text{TC, total cholesterol; LDL-C, LDL-cholesterol; HDL-C, HDL-cholesterol; OX-LDL, oxidised LDL-cholesterol.}

\(^a\)Mean values with unlike subscript upper-case letters were significantly different from baseline in the placebo group at the intra-group level (P < 0.05).

\(^b\)Mean values with unlike subscript lower-case letters were significantly different from baseline in the L. plantarum group at the intra-group level (P < 0.05).

\(^*\)P value indicates significant inter-group differences.

A more profound analysis of the results showed that in patients with HIV of TC, the reduction in TC and LDL-C after 12 weeks of consumption compared with the baseline values was higher than in patients with HIV of TC (17-4% and 17-6% v. 9-4 and 11-5%, respectively). This finding may suggest that patients with higher levels of TC may benefit from higher reductions in TC and LDL-C after treatment with L. plantarum than after any others. Therefore, the biofunctionalit of L. plantarum could be proportional to the cardiovascular risk of the patient.

Finally, the analysis of safety parameters did not show any deleterious effects associated with L. plantarum consumption. Therefore, L. plantarum AB-LIFE™ could fulfil all the requirements of safety and efficacy in the treatment of hypercholesterolaemia.

L. plantarum (CECT 7527, CECT 7528 and CECT 7529) strains may reduce cholesterol levels by different mechanisms (M Bosch, MC Fuentes, S Audvert, MA Bonachera, S Peiro and J Cuñé; unpublished results): favouring the reduction of plasma cholesterol through the reduction of the enterohepatic circulation of bile salts (due to the bile salt hydrolase activity); reducing the bioavailability of cholesterol from the diet; producing large quantities of propionic acid which can then cause a decrease in the systemic levels of blood lipids by inhibiting hepatic cholesterol synthesis and/or redistributing cholesterol from the plasma to the liver\(^\text{21}\); producing large quantities of butyric acid, which is an important source of energy for the colonocytes\(^\text{22}\). Bile salt hydrolase activity allows the strains to be able to metabolise the bile salts excreted by the gallbladder during digestion, thereby preventing their reabsorption\(^\text{23}\). As a consequence, the liver requires a higher mobilisation of systemic cholesterol for the de novo synthesis of bile salts for the next digestive cycle, favouring a major reduction in plasma cholesterol. It is known that some drugs that are used in the treatment of

\[ \text{P} \quad \text{NS} \quad \text{P} \quad \text{NS} \quad \text{P} \quad \text{NS} \quad \text{P} \quad \text{NS} \]
hypercholesterolaemia may cause many adverse side effects, sometimes dangerous(24). There are other possibilities of treatment, especially when the increase in LDL-C is not very high. In these situations, clinicians often use dietary phytosterols. Phytosterols lower blood concentrations of cholesterol by inhibiting intestinal absorption of cholesterol by mean of competing for the cholesterol space in mixed micelles, which are the form of lipid delivery for absorption into the mucosal cells(25). Taken into account that approximately 25% of the plasma cholesterol production rate is due to absorbed dietary cholesterol and 75% is accounted for by endogenously synthesised cholesterol(26), the effect of phytosterol on circulating LDL-cholesterol could be limited. Moreover, the consumption of high doses of plant sterols significantly reduces the blood levels of carotenoids and, to a lesser extent, of other essential fat-soluble nutrients(27). This is why European Union regulations limit exposure to a maximum of 3 g/d in order to avoid intakes above the recommended limits(27).

Considering these topics, new therapies that combine efficacy and safety could be useful for many patients. L. plantarum (CECT 7527, CECT 7528 and CECT 7529) is safe at high doses, affects dietary cholesterol but mostly affects L. plantarum hypercholesterolaemia. CECT 7527, CECT 7528 and CECT 7529 seem to be a safe and superior alternative to traditional probiotic therapy in the treatment of hypercholesterolaemia.

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