



Meta-analysis and narrative review confirm the benefit of essential phospholipids in non-alcoholic fatty liver disease

Lorena Petcu, MD, and Branko Popovic, MD

Non-alcoholic fatty liver disease (NAFLD), also known as metabolic associated fatty liver disease or MAFLD, is one of the most common liver diseases worldwide. Although NAFLD is associated with metabolic risk factors, up to 40% of patients with NAFLD are not obese but can still be considered metabolically unhealthy. Current treatment recommendations for NAFLD focus on lifestyle interventions (weight loss, diet, exercise) since there are few if any accepted pharmacologic therapies. Essential phospholipids (EPLs) are recommended by some therapy guidelines as supportive treatment. A meta-analysis has now provided evidence to support this recommendation.

Previous focus on treatment of comorbidities

Due to its steadily rising prevalence, NAFLD poses a significant health problem. 25% to 30% of the adult population is thought to be living with NAFLD. Current treatment largely focuses on lifestyle changes and the treatment of comorbidities such as diabetes mellitus, insulin resistance, obesity, hypertension, and dyslipidaemia. Some guidelines suggest the use of pioglitazone (off-label for non-diabetic patients), but at the same time draw attention to safety concerns [1, 3].

EPLs currently the most promising adjunctive treatment option

Some recently published therapeutic guidelines recommend limiting the damage to the liver by administering “hepatoprotective” medicinal products [1–3]. **Figure 1** from a recent narrative review [4] presents a schematic diagram summarising the currently available data concerning the efficacy of and the evidence for different hepatoprotective agents in the treatment of NAFLD. As can be seen from Figure 1, no convincing data exists for ursodeoxycholic acid (UDCA), vitamin D, resveratrol, Phyllanthus, garlic, coenzyme Q10 (ubiquinone), ademetionine, milk thistle seed extract (silymarin) or glycyrrhizic acid concerning their efficacy in NAFLD. There are indications of a therapeutic effect for metadoxine and artichoke, but the evidence level here is low. However, vitamin E (potentially combined with vitamin C) and essential phospholipids (EPLs) show positive effects for which there is a high level (Vit. C) or medium

level (EPLs) of evidence. For vitamin E, though, there is an increased risk of side effects following longer-term use of high doses (symbolised by the asterisk in Fig. 1) [4]. This makes EPLs medicinal products currently the most promising (adjuvant) therapy option for NAFLD.

Meta-analysis confirms benefit of EPLs

A recent meta-analysis [5] comprehensively investigated the state of knowledge concerning the use of EPLs in patients with NAFLD. Although many of the analysed studies are relatively small, in total they provide several pieces of evidence indicating the therapeutic benefit of EPLs in NAFLD. In nearly all studies, EPLs – either on their own or as part of combination therapy – improved the course of the disease. NAFLD patients with type 2 diabetes and/or obesity profited from the administration of EPLs by a reduction of alanine aminotransferase (ALT; **Fig. 2A**), triglyceride (**Fig. 2B**), and cholesterol levels (**Fig. 2C**), and experienced an improvement in the severity of the disease (**Fig. 2D**) [5]. Most studies lasted at least several months, providing evidence for the safety of EPLs with longer-term use.

Significant benefit

When compared to antidiabetic therapy alone, the meta-analysis showed that a combination of antidiabetic therapy with EPLs is more likely to improve the overall disease while reducing the probability of developing severe steatosis. The aggregated estimated value for the proportion of patients showing clinical improvement was 87%, based on data from

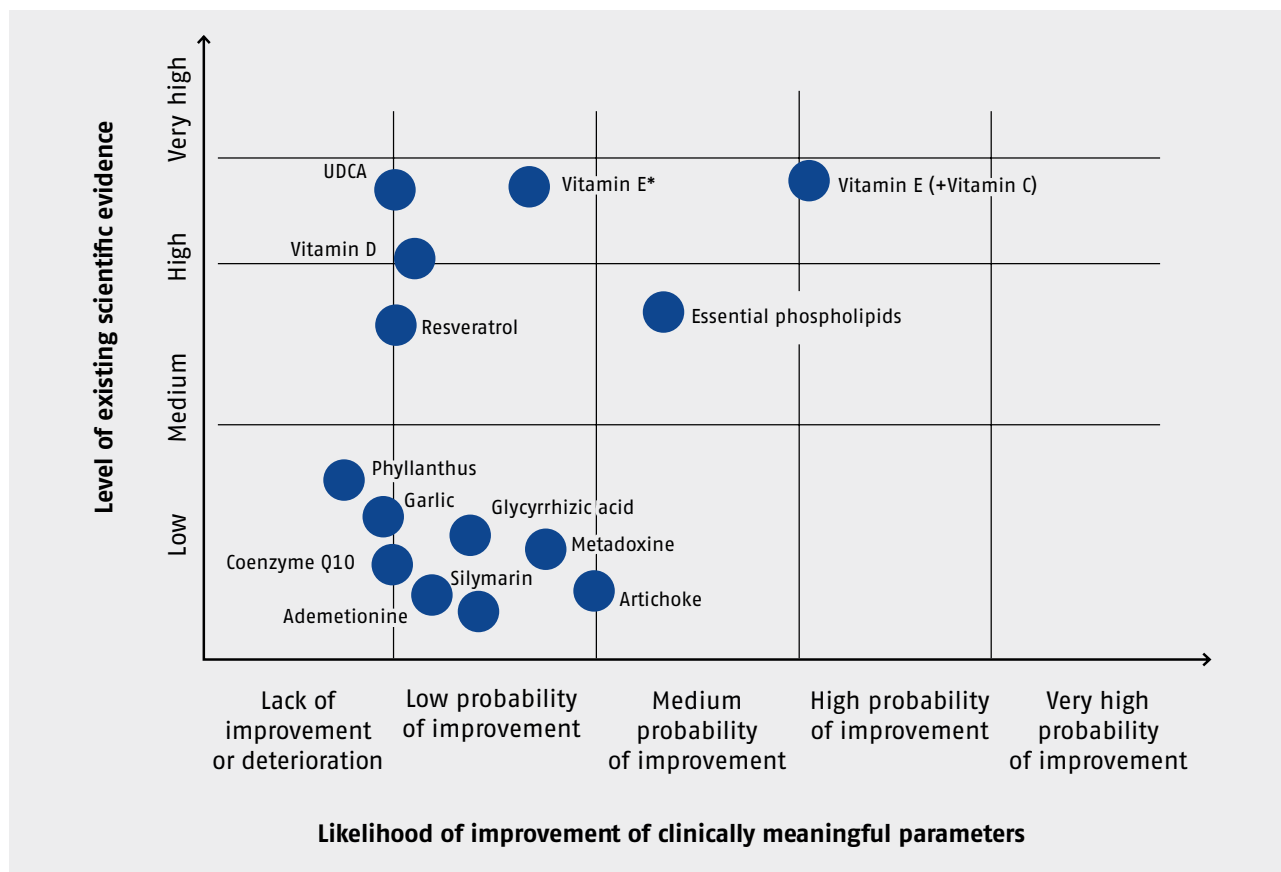


Fig. 1. Schematic diagram on the available data concerning the efficacy of and the evidence for different hepatoprotective agents in the treatment of NAFL [4]. * long-term use of high doses

three studies (n = 205) over a mean duration of 2.47 months. The aggregated estimated value for the proportion of patients showing significant clinical improvement was 58%, based on data from four studies (n = 357) with a mean duration of 3.97 months.

Overall, the meta-analysis [5] provided good evidence of beneficial effects of EPLs in NAFLD patients with diabetes and/or obesity. Administration of EPLs is already recommended for NAFLD in Russian [2] and Latvian [3] guidelines. Based on the data presented here, additional countries could soon follow.

Literature

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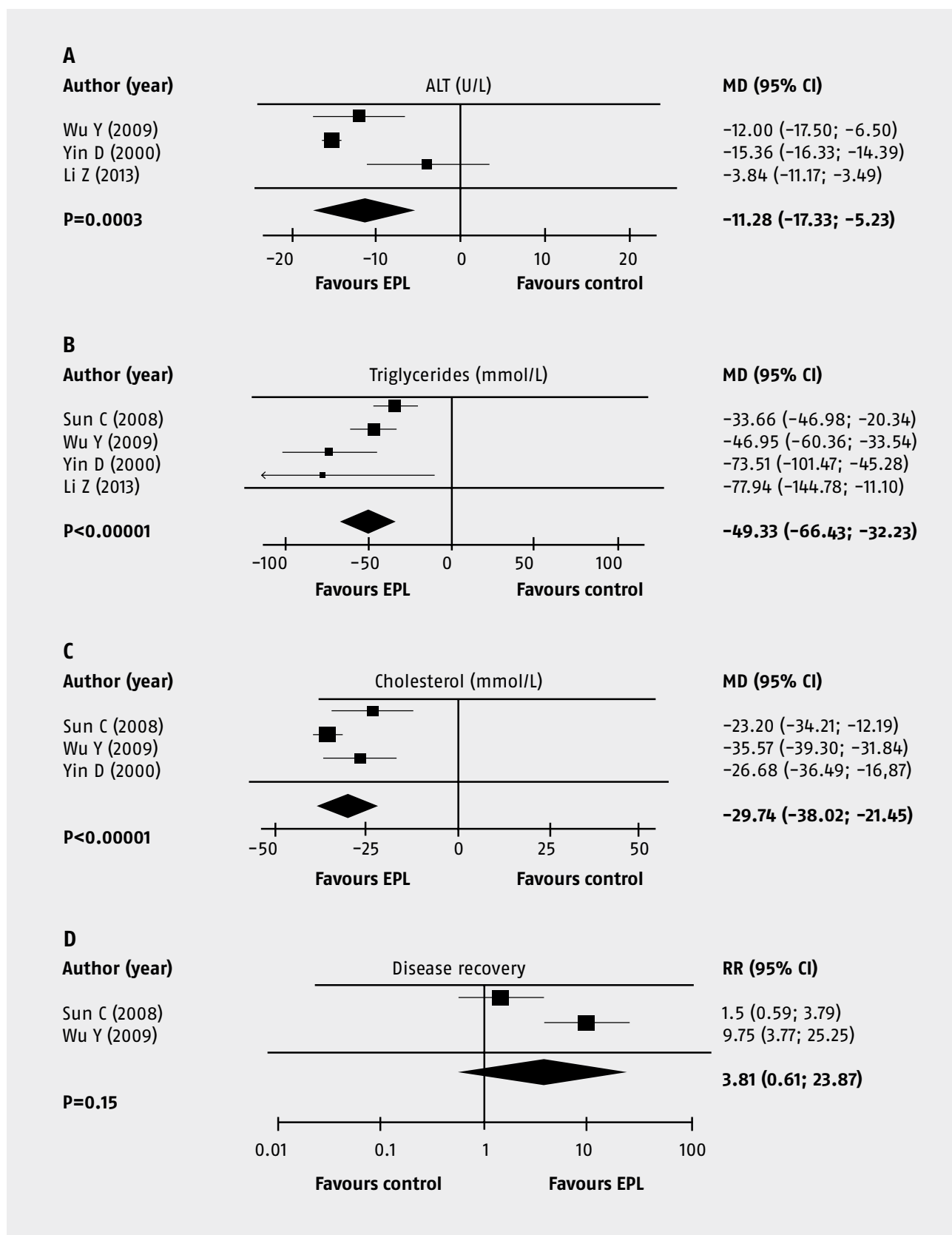


Fig. 2. Results of the direct meta-analyses (random effects model) of randomized controlled trials comparing EPLs and antidiabetic therapy with antidiabetic therapy (control). A: Change in alanine aminotransferase levels; B: Change in triglyceride levels; C: Change in total cholesterol levels; D: Relative risk of recovery [5]

MD: Mean difference; CI: Confidence interval; RE: Random effects; RR: Relative risk; ALT: Alanine aminotransferase.