



Essential phospholipids. Mechanism of action in liver disease explained



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Flash for webinar (~20 mins)

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Phospholipids in the liver

The liver is responsible for around 500 bodily functions, including digestion, nutrient storage, protein synthesis, detoxification and metabolism.¹ Liver cells (hepatocytes) have membranes comprising primarily of a bilayer of phospholipids (PL), which influence their fluidity, integrity, and function.² In particular, phosphatidylcholine (PPC) is the most abundant form of PL in the cell membranes of hepatocytes.^{2,3}

Essential phospholipids (EPL)

EPL supplements are indicated for liver diseases of various origins. They contain PPC derived from highly purified soybean extract. The main active ingredient is 1,2-dilinoleoylphosphatidylcholine (DLPC), which differentiates EPL from phospholipids derived from the diet.³ "Essential" in EPL refers to essential fatty acids comprising the acyl moieties of the polyunsaturated phospholipids.³

Of five commercially available EPL preparations, Essentiale® Forte® has been found by comparative analysis to have the highest phosphatidylcholine (PtdCho) levels (61.9 mol%) and lowest phosphatidylethanolamine (PtdEtn) levels (4.9 mol%). It might therefore be considered that Essentiale® Forte® is the most beneficial of the available hepatoprotective NAFLD treatments.⁴

Essentiale® Forte: Mechanism of Action

EPL increase hepatocyte membrane fluidity and counter the effects of increased cellular cholesterol in liver disease by modifying membrane lipid composition in a way that protects against the development of insulin resistance,⁵⁻⁷ and demonstrate an anticholestatic effect.^{8,9} They also exert detoxification effects including inhibition of lipid peroxidation,^{10,11} reduce liver steatosis, fibrosis and cirrhosis,¹²⁻¹⁵ and stimulate liver regeneration.¹⁶⁻¹⁸

Study of the effects of PPC on the biochemical processes in hepatocytes suggests that EPL have multiple modes of action in liver diseases. Upregulation of beta-oxidation of fatty acids,¹⁹ and contribution to the formation of very low-density lipoproteins (VLDL)²⁰ aids elimination of lipids from the hepatocyte.^{19,21} Inhibition of triglyceride synthesis proteins helps reduce the quantity of lipids in liver cells.²²

EPL: essential phospholipids; **NAFLD:** non-alcoholic fatty liver disease; **NASH:** non-alcoholic steatohepatitis; **HCC:** hepatocellular carcinoma; **ALD:** alcoholic liver disease; **CHC:** chronic hepatitis; **HRQoL:** health related quality of life.

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EPL have multiple modes of action in liver diseases	
Restore cell membrane structure	Stimulate liver regeneration
Increase cell membrane fluidity	Correct or inhibit fibrogenic processes
Enhance membrane-associated metabolic functions	Influence apoptosis
Reduce or normalise peroxidative reactions	Stabilise bile composition
Decrease cytolysis	Modulate lipid metabolism
Improve excretory, detoxifying/clearing, and synthesizing capacity of the liver	Diminish or abolish fatty infiltration and hepatocyte necrosis
Improve immune properties	Decrease experimental hepatocarcinogenesis

Clinical Efficacy of EPL

Evidence from clinical studies has demonstrated the efficacy of EPL in the management of NAFLD/NASH with or without T2DM. They have been shown to improve liver structure by decreasing the progression of fatty infiltration of the liver and slowing down hepatic fibrogenesis and steatosis,^{3,13} reduce liver size and improve liver function through a reduction in transaminase levels,²³ reduce triglycerides and cholesterol levels,²⁴ and improve clinical status.²³

Essentiale® Forte® has displayed statistically significantly greater benefit, variously relative to placebo, inosine+vitamin C, vitamin E, or vitamin therapy, with respect to the following endpoints: ALT, AST, response rate, histology, ultra-sonography, and reported symptoms.²⁵⁻²⁹

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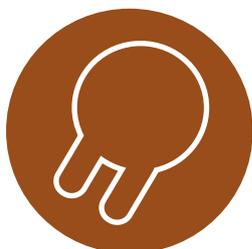
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References

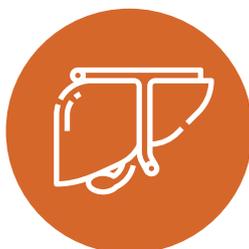
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What does a NAFLD patient journey look like? Importance of HR-QoL

Learning objectives:



Understand the roles of phospholipids in hepatocytes and the key characteristics and composition of EPL.

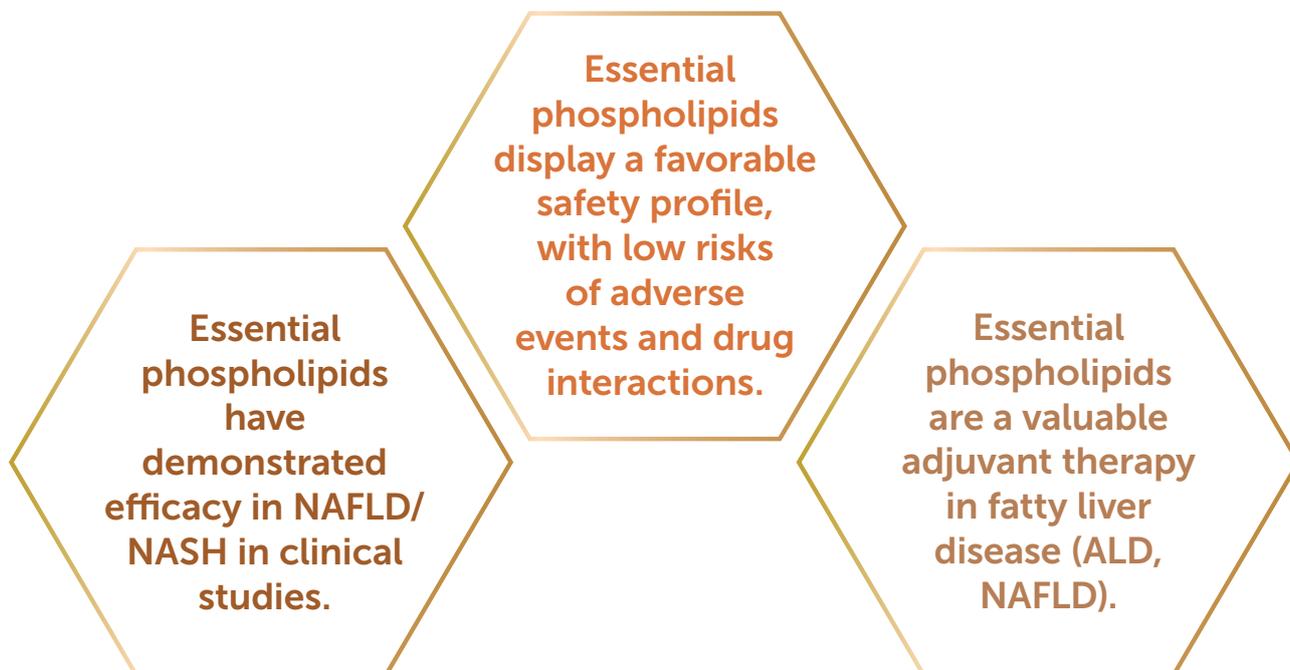


Review the pre-clinical evidence for EPL in liver disease and understand their pleiotropic mechanisms of action.



Describe clinical evidence that supports the use of EPL in the management of patients with fatty liver disease with and without type 2 diabetes.

Main take aways:



The logo features a stylized liver shape with a hexagonal pattern, transitioning from orange to red. The text "1st GLOBAL LIVER HEALTH FORUM" is written in white, bold, sans-serif font over the liver shape.

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