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Preserving Phosphatidylcholine Integrity in a High-Stability Soy Lecithin Softgel System: Implications for Hepatic Lipid Homeostasis

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Abstract: Phosphatidylcholine (PC) is a major hepatocyte phospholipid and a choline-bearing substrate for membrane renewal and lipoprotein assembly. We evaluated a stabilized soybean-lecithin softgel and placed its physicochemical performance beside human evidence on choline and phosphatidylcholine in hepatic physiology. The NVTIA® fill contains 75.00% fluid soybean lecithin, 24.52% caprylic/capric triglyceride, 0.34% mixed tocopherols, and 0.14% L-ascorbyl palmitate. Processing used low-temperature vacuum dehydration, nitrogen-protected mixing, vacuum degassing, and filtration. After 30 days at 40°C/75% relative humidity, the optimized system retained 96.4% PC, with a peroxide value of 3.5 mmol/kg and 0.8% oil leakage. Comparator formulations that removed antioxidant protection, changed the carrier oil, or increased moisture/oxygen exposure showed lower PC retention and/or higher peroxide values. Human feeding studies show that choline availability is necessary for hepatic integrity, and contemporary MASLD trials of essential phospholipids or phosphatidylcholine report changes in steatosis, liver biochemistry, oxidative-stress measures, or related metabolic endpoints. The experimental result is therefore a delivery result: the formulation maintains a defined choline-bearing phospholipid matrix over storage. That platform can be taken forward into pharmacokinetic and liver-focused human studies with verified PC exposure.

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1. Introduction

Phosphatidylcholine is both a structural membrane lipid and a metabolic intermediate. Its choline moiety links phospholipid turnover with one-carbon metabolism and lipid export from the liver [1]. Human work has established choline as an essential nutrient [2], and controlled feeding experiments show marked inter-individual variation in the amount required to avoid hepatic or muscle dysfunction [3]. Genetic variation contributes to that susceptibility [4], while low-choline feeding has also been associated with greater lymphocyte DNA damage/apoptosis and distinct gene-expression responses in those who develop organ dysfunction [5], [6].

For a lecithin product, nominal phospholipid content is only part of the exposure question. Fluid soybean lecithin contains unsaturated phospholipids and associated neutral lipids that are sensitive to oxygen, heat, and residual water. Oxidative deterioration

can raise peroxide formation and alter the amount of native phospholipid present at the time of use. Softgel manufacture adds a practical constraint because highly viscous or moisture-rich fills are more difficult to encapsulate and may leak during storage.

The NVTIA® system addresses those issues with MCT as a relatively oxidation-resistant carrier and viscosity modifier, mixed tocopherols plus L-ascorbyl palmitate as lipid-phase antioxidants, and vacuum/nitrogen processing to limit water and oxygen exposure. The formulation was evaluated as a stabilized phospholipid matrix rather than as a simple dilution of lecithin.

The experiments focused first on moisture, viscosity, peroxide value, PC retention, and leakage after accelerated storage. Human hepatic studies were then used as a separate evidence layer to identify relevant physiological endpoints. Keeping those two layers distinct allows formulation quality to be characterized directly while the liver literature guides subsequent exposure and outcome measurements.

2. Materials and Methods

2.1 Formulation and preparation

The optimized oil phase contained 75.00% fluid soybean lecithin, 24.52% caprylic/capric triglyceride, 0.34% mixed tocopherols, and 0.14% L-ascorbyl palmitate. Starting lecithin contained 62.1% acetone-insoluble matter, 15.4% PC, 0.62% moisture, and a peroxide value of 2.2 mmol/kg. The MCT contained 97.3% combined caprylic and capric triglycerides, with an acid value of 0.18 mg KOH/g, an iodine value of 0.4 g I₂/100 g, and a peroxide value of 0.3 mmol/kg.

Table 1. Composition of the optimized phospholipid softgel fill

Component	Optimized level (w/w)	Functional role in system
Fluid soybean lecithin	75.00%	Primary phospholipid/PC matrix
Caprylic/capric triglyceride	24.52%	Viscosity control; oxidation-resistant carrier
Mixed tocopherols	0.34%	Lipid-phase antioxidant
L-ascorbyl palmitate	0.14%	Complementary lipid-phase antioxidant

2.2 Comparative design and analytical endpoints

MCT was heated to 52°C under nitrogen before L-ascorbyl palmitate and mixed tocopherols were added. Fluid soybean lecithin was dehydrated at 45°C under -0.090 MPa vacuum for 30 min; moisture after dehydration was 0.28%. The lecithin was cooled to 42°C and blended with the antioxidant oil phase while headspace oxygen was maintained at or below 5.0%. Mixing proceeded at 90 r/min for 30 min with material at 41-42°C. The fill was then vacuum-degassed at -0.085 MPa for 15 min and filtered through 100 mesh.

2.3 Human evidence integration

Six comparators altered one formulation or process feature: untreated fluid lecithin; soybean oil in place of MCT; omission of both antioxidants; mixed tocopherols without L-ascorbyl palmitate; omission of vacuum dehydration and nitrogen protection with 60°C mixing; and addition of 1.0% 30% ethanol-water solution. Moisture was measured by Karl Fischer volumetry, viscosity at 40°C by rotational viscometry, peroxide value by iodometric titration, and PC by normal-phase HPLC with evaporative light-scattering detection. Softgels contained 750 mg fill, and 1000 capsules per formulation were examined for visible oil leakage after 30 days at 40°C/75% relative humidity.

The human-evidence search focused on soy lecithin, phosphatidylcholine, essential phospholipids, and choline in hepatic lipid accumulation, liver enzymes, oxidative stress, and controlled depletion/repletion. Randomized or placebo-controlled trials and

prospective clinical studies received priority. The published results were used to select biological endpoints; they were not combined statistically with the formulation data.

3. Results

3.1 Formulation performance

The optimized fill contained 0.23% moisture and had a viscosity of 4050 mPa·s at 40°C. After accelerated storage, its peroxide value was 3.5 mmol/kg, PC retention was 96.4%, and oil leakage was 0.8%. Untreated lecithin had a viscosity of 9100 mPa·s, retained 89.7% PC, reached 6.8 mmol/kg peroxide value, and showed 3.8% leakage. Without both antioxidants, PC retention was 90.8% and peroxide value 5.8 mmol/kg. Tocopherols alone gave 92.9% PC retention and 4.8 mmol/kg peroxide value. The soybean-oil carrier comparator retained 92.1% PC and reached 5.4 mmol/kg.

Process conditions produced their own differences. Without vacuum dehydration and nitrogen protection, and with mixing at 60°C, the fill contained 0.54% moisture, retained 91.8% PC, and leaked in 2.6% of capsules. Adding the ethanol-water phase increased moisture to 0.78% and leakage to 2.3%. These data show that water removal, oxygen control, carrier choice, and antioxidant composition all changed the stored matrix.

Table 2. Comparative physicochemical performance of the optimized and comparator formulations.

Formulation	Moisture (%)	Viscosity at 40°C (mPa·s)	PV 30 d (mmol/kg)	PC retention (%)	Oil leakage (%)
Optimized formulation	0.23	4050	3.5	96.4	0.8
Untreated lecithin	0.62	9100	6.8	89.7	3.8
Soybean-oil carrier	0.24	4850	5.4	92.1	1.5
No antioxidants	0.24	3980	5.8	90.8	1.0
Tocopherols only	0.23	4050	4.8	92.9	0.9
No dehydration/N ₂ ; 60°C mixing	0.54	4240	5.1	91.8	2.6
1% ethanol-water	0.78	4620	5.0	92.4	2.3

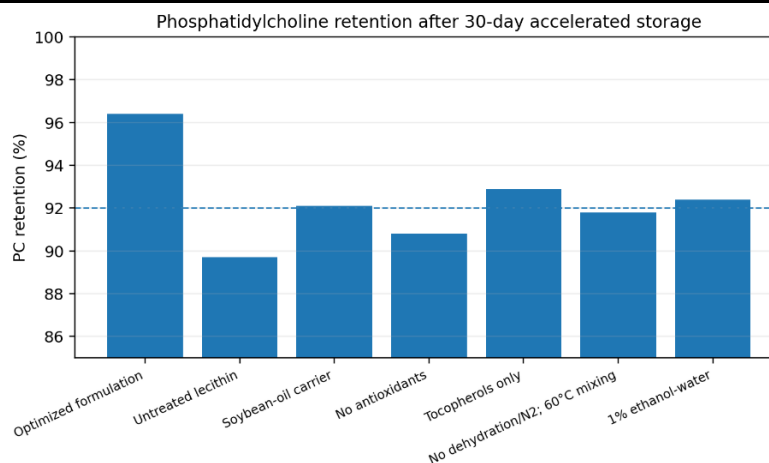


Figure 1. Phosphatidylcholine retention after accelerated storage; dashed line indicates the 92% reference threshold used in the formulation specification

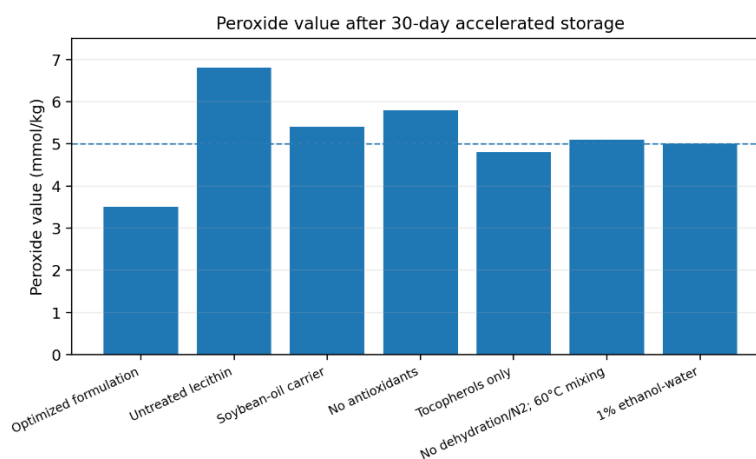


Figure 2. Peroxide value after 30-day accelerated storage; dashed line indicates 5.0 mmol/kg.

3.2 Human evidence context

Human studies supply several distinct liver endpoints. In the 2026 multicenter phase IV trial, 193 participants with MASLD and cardiometabolic comorbidity were randomized and 165 entered the modified intention-to-treat population; essential phospholipids improved the CAP steatosis measure at six months versus placebo [7]. Sedhom et al. used phosphatidylcholine 2400 mg/day for 12 weeks and reported lower CAP values together with changes in liver enzymes, oxidative-stress measures, and triglycerides [8]. Manuc et al. compared essential phospholipids with silymarin in MASLD and reported favorable biochemical and liver-stiffness findings in the phospholipid arm [9]. Abenavoli et al. also examined phosphatidylcholine prospectively in NAFLD [10]. Earlier work in long-term parenteral-nutrition patients showed that oral lecithin increased plasma free choline and was associated with progressive reduction of hepatic steatosis [11], while placebo-controlled choline repletion demonstrated reversible hepatic abnormalities in deficiency [12].

Table 3. Selected human studies relevant to hepatic phospholipid/choline physiology

Study	Population	Intervention	Principal reported finding
Stefan et al., 2026 [7]	193 randomized; MASLD + cardiometabolic risk	Essential phospholipids vs placebo, 6 mo	CAP improved vs placebo; fatigue and HbA1c also improved
Sedhom et al., 2025 [8]	79 NAFLD patients randomized	PC 2400 mg/d + conventional care vs care, 12 wk	Lower CAP; favorable liver enzyme, oxidative-stress and TG findings
Manuc et al., 2024 [9]	90 randomized; 68 completed	EPL 825 mg bid vs silymarin, 6 mo	Favorable biochemical and liver-stiffness changes in EPL arm
Buchman et al., 1992 [11]	15 long-term TPN patients	Oral lecithin vs placebo, 6 wk	Plasma choline +53.4% at 2 wk; progressive CT evidence of reduced hepatic fat
Fischer et al., 2007 [3]	57 healthy adults, controlled feeding	Choline depletion then graded repletion	Fatty liver/muscle damage developed in many men and postmenopausal women

4. Discussion

The 96.4% PC retention did not arise from one isolated excipient. The optimized matrix combined lower residual water, limited oxygen exposure, MCT as the carrier, and two antioxidants. Removing antioxidants increased peroxide formation; replacing MCT with soybean oil increased oxidative load; and omitting dehydration/nitrogen protection reduced chemical stability and capsule performance. The stored product therefore reflects formulation-process coupling rather than a single protective step.

That delivery result is relevant to a liver study because phosphatidylcholine is part of the biological exposure, not an inert carrier. Human depletion experiments show that lowering choline availability can precipitate liver or muscle dysfunction in susceptible adults and that requirements differ by sex and genotype [2]-[6]. The present softgel does not reproduce those depletion experiments; it supplies a better-defined starting matrix for studying the opposite side of the pathway—verified choline-bearing phospholipid exposure.

The recent MASLD trials use clinically contemporary endpoints. Stefan et al. measured CAP in a multicenter placebo-controlled design [7], Sedhom et al. included steatosis, liver enzymes, oxidative stress, and triglycerides [8], and Manuc et al. assessed biochemical and stiffness-related outcomes [9]. Older lecithin and choline work contributes a different type of evidence because it directly demonstrates changes in circulating choline and hepatic integrity [11], [12]. A phosphatidylcholine intervention in healthy men also altered homocysteine handling, confirming that oral PC can modify a measurable downstream choline-dependent pathway [13].

The formulation experiment answers a narrower question: can a phospholipid-rich softgel maintain its intended composition during manufacture and storage? High PC retention, practical viscosity, and low leakage mean that subsequent pharmacokinetic or liver studies can start with a better-characterized intervention. A 2024 randomized pharmacokinetic study of soy-derived lysophosphatidylcholine illustrates the value of measuring molecular choline exposure directly after ingestion [14].

Mixed tocopherols and L-ascorbyl palmitate were used as complementary lipid-phase antioxidants, and the tocopherol-only comparator did not preserve PC as well as the dual-antioxidant system. MCT contributed both to viscosity control and to a lower burden of unsaturated carrier lipid. Those are formulation functions. The liver hypothesis remains centered on delivery of the choline-bearing phospholipid matrix.

For translation, the sequence can be kept simple: verify composition, measure exposure, then measure physiology. Plasma choline and phosphatidylcholine species can be quantified after the stabilized softgel before moving to longer studies of hepatic steatosis, liver enzymes, lipid transport, or patient-centered outcomes. The EFSA review of choline is consistent with the established roles of choline in normal lipid metabolism and liver function [15], but a product-specific study still benefits from measuring the complete NVTIA® intervention directly.

4.1 Study Considerations and Future Directions

Real-time shelf-life testing and phospholipid-species profiling by LC-MS would extend the current stability work. A single-dose study can then measure postprandial choline-containing metabolites from the stabilized softgel. Longer prospective studies may use CAP or other imaging, liver enzymes, lipid-transport markers, and prespecified clinical outcomes. Baseline choline status, sex, menopausal status, and relevant genetic variation should be recorded because controlled feeding studies show substantial variation in choline requirements [3], [4].

5. Conclusion

The stabilized soy-lecithin softgel retained 96.4% phosphatidylcholine after 30 days at 40°C/75% relative humidity while maintaining 4050 mPa·s viscosity and 0.8% leakage. Comparator data show that antioxidant composition, carrier choice, water removal, and oxygen control each affect the stored phospholipid matrix. Human studies establish a clear hepatic choline-phosphatidylcholine pathway and supply clinically useful endpoints ranging from choline exposure to steatosis and liver biochemistry. The next step is to connect the verified NVTIA® phospholipid exposure with those endpoints in formulation-specific human studies.

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