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INPLASY

# Effectiveness of Phospholipid-Encapsulated Iron Supplements as Alternatives to Conventional Iron Supplements in Terms of Iron Status: A Systematic Review

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## ADMINISTRATIVE INFORMATION

**Support -** No financial support.

**Review Stage at time of this submission -** Formal screening of search results.

**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY202660122

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 June 2026 and was last updated on 22 October 2026.

## INTRODUCTION

**Review question / Objective** Are liposomal or sucrosomial iron formulations effective as an alternative to conventional iron supplements in terms of iron status for all groups of people, with or without iron-deficiency-anemia (IDA) or non-anaemic-iron-deficiency (NAID), and without any underlying medical condition like for example CKD, IBD, Celiac Desease or Oncology? Can those formulations be seen as an alternative to conventional ones? What does the study situation say about that? Effectiveness measured in change of known blood parameters for iron status and anaemia. Possible side effects (mainly gastroenterological) compared to conventional supplements?

**Condition being studied** Effectiveness of Sucrosomial® and various Liposomal Iron Supplements, review of the study situation.

## METHODS

**Search strategy** The search was extended to five databases (PubMed, ScienceDirect, Springer Nature Link, Web of Science and Wiley Online Library) and covered the period up to and including 3 August 2026, without filters for publication date, publication type or language. Titles and, where available, abstracts and keywords were searched with predefined terms combined with Boolean operators. The core terms were "liposomal iron", "sucrosomial iron", "microsomal iron", "micronised AND dispersible AND iron", "micronised AND microencapsulated AND iron", "iron pyrophosphate NOT citrate", "ferric pyrophosphate NOT citrate" and "ferrous pyrophosphate NOT citrate", together with the product names SiderAL, SunActive, LipoCellTech, Lipofer, FerFer, Turbofer and LiposoVit. The operator "NOT citrate" was used to exclude ferric pyrophosphate citrate, which is used as a dialysate in chronic kidney

disease. Common spelling variants and synonyms (e.g. liposomic, liposomial, sucrosomic, sucrosomal, microsomial, ferrum) were also searched. In addition, results from Google Scholar were screened manually and non-systematically, and ClinicalTrials.gov was searched non-systematically for registered trials. Titles, abstracts and full texts were screened independently by two reviewers, and discrepancies were resolved by discussion.

**Participant or population** Participants of any age and sex were eligible, including infants, children, adolescents and adults, as well as pregnant, postpartum and lactating women, menstruating women and pre- and postmenopausal women. Studies including participants without anaemia or iron deficiency, with non-anaemic iron deficiency (NAID) or with iron-deficiency anaemia (IDA) were all eligible. Populations with underlying conditions that directly affect iron absorption, utilisation or regulation, such as chronic kidney disease, inflammatory bowel disease, coeliac disease or cancer, remained excluded. In addition, populations with genetically determined anaemias or disorders of iron metabolism (e.g. thalassaemia, sickle cell disease) and bariatric or other surgical populations in which the surgery interfered with the iron treatment (e.g. after cardiac surgery) were excluded. Studies in which iron was given before elective surgery remained eligible.

**Intervention** Orally administered Sucrosomial® iron (SI) or liposomal iron (LI), alone or combined with vitamin C. Products reported as LI included formulations described as liposomal, micronised or microencapsulated ferric pyrophosphate.

**Comparator** Conventional oral iron, intravenous iron, placebo, or no supplementation or standard care. Studies without a control group (single-arm or before-and-after designs) were also eligible.

**Study designs to be included** RCT, CT, non-controlled intervention trials, observational trials, pilot trials.

**Eligibility criteria** Human studies of orally administered Sucrosomial® iron (SI) or liposomal iron (LI) were eligible, including products containing vitamin C. Eligible comparators were conventional oral iron, intravenous iron, placebo, and no supplementation or standard care, and studies without a control group were also included. Studies had to report at least one haematological or iron-status laboratory parameter, such as haemoglobin, serum ferritin or transferrin saturation. The following exclusions were added or specified after registration. Studies assessing only subjective endpoints were excluded, as were retrospective observational studies reporting only a single, isolated iron-status parameter without a baseline, endpoint or comparator value. Populations with genetically determined anaemias or disorders of iron metabolism (e.g. thalassaemia, sickle cell disease) and bariatric or other surgical populations in which the surgery interfered with the iron treatment were also excluded. Reviews were not included in the study selection. The exclusion of iron-fortified foods and of combination products containing vitamin B12, folate, vitamin B6 or other nutrients relevant to haematopoiesis remained unchanged.

**Information sources** PubMed, ScienceDirect, Springer Nature Link, Web of Science and Wiley Online Library, searched up to and including 3 August 2026. In addition, Google Scholar were screened manually and non-systematically, and ClinicalTrials.gov was searched non-systematically for registered trials of SI and LI.

**Main outcome(s)** Change in haemoglobin (Hb) and serum ferritin (SF) from baseline to the end of supplementation, within groups and compared with the respective comparator.

**Additional outcome(s)** Transferrin saturation and further haematological and iron-status parameters, such as red blood cell count, haematocrit, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, soluble transferrin receptor and C-reactive protein, as well as gastrointestinal tolerability and other adverse events.

**Data management** Records retrieved from the databases were combined, and duplicates were removed before screening. Titles, abstracts and full texts were screened independently by two reviewers, and reasons for exclusion at the full-text stage were documented. For each included study, a standardised set of variables was extracted by one reviewer and checked by a second reviewer. These included study design, country, population, intervention and comparator (iron formulation, dose and route of administration), group sizes, study duration, all reported outcomes and results, and information on gastrointestinal tolerability.

**Quality assessment / Risk of bias analysis** Risk of bias was assessed for the main outcomes haemoglobin and serum ferritin. Randomised controlled trials were assessed with the revised Cochrane risk-of-bias tool for randomised trials (RoB 2, version of 22 August 2019), and non-

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randomised studies with the Risk Of Bias In Non-randomised Studies of Interventions tool (ROBINS-I, original 2016 version). The assessment focused on the effect of assignment to the intervention and on the end-of-treatment results. Both outcomes were rated together, as they are objective laboratory values obtained from the same blood samples. The ratings were performed by one reviewer and independently checked by a second reviewer, and disagreements were resolved through discussion. No study was excluded on the basis of the risk-of-bias ratings, and the results were taken into account when interpreting the findings.

**Strategy of data synthesis** No meta-analysis was performed because the included studies differed considerably in population, study design, iron formulation, dose, comparator, outcome parameters and duration of supplementation. The results were synthesised narratively. Studies were grouped into six categories by iron formulation (SI or LI) and population (adults, pregnant and postpartum women, children and infants). Within each category, the results for haemoglobin and serum ferritin and, where reported, transferrin saturation and further haematological parameters were compared, recording the direction of change within and between groups and the statistical significance reported by the authors. Effect sizes were not recalculated. Results were interpreted separately for each type of comparator, taking into account the elemental iron dose in each study arm. Gastrointestinal tolerability and other adverse events were summarised descriptively.

**Subgroup analysis** None reported.

**Sensitivity analysis** None reported.

**Language restriction** Main Language: English, but no language is excluded.

**Country(ies) involved** Germany.

**Other relevant information** The following amendments were made after registration. The title was adapted, and two co-authors (Andreas Rummel and Kim Ohl) were added. The search was extended to five databases, Google Scholar and ClinicalTrials.gov, covering the period up to 3 August 2026. The eligibility criteria were specified as described above, and the outcomes, risk-of-bias assessment and synthesis strategy were completed.

**Keywords** liposomal iron; sucrosomial iron; ferric pyrophosphate; iron deficiency; iron-deficiency anaemia; non-anaemic iron deficiency; oral iron supplementation; ferritin; gastrointestinal tolerability; systematic review

**Dissemination plans** The results will be submitted for publication in Nutraceuticals (MDPI), a peer-reviewed open-access journal

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