

Comparison of Morphological Analysis of Two Different Products Based on Iron Pyrophosphate

Abstract

In this work we present the comparison between the Lipofer of Lipofoods-Lubrizol and the pyrophosphate iron produced by Lipotech Argentina.

Our aim is demonstrating the morphological differences of the two products, examined by microscopy and granulometry instruments, and their different supposed effectiveness resulting from it.

In a future work we are going to compare the effectiveness of the two products with clinical studies conducted on a wide range of cases.

Keywords: Iron pyrophosphate; Microencapsulation; Morphological examinations

Received: July 14, 2021; **Accepted:** July 22, 2021; **Published:** July 31, 2021

Introduction

Iron deficiency and anemia, definition

Iron deficiency is a condition in which iron availability is insufficient to meet the body's needs and which can co-exist with or without anemia. It depends on insufficient iron intake or defective metabolism [1]. It is very frequent and widespread both in industrialized and not industrialized country. It represents the only nutritional disorder, significantly prevalent in developed countries, affecting over 2 million people (about over 30% of the world population is anemic) [2]. Iron is an essential element that is needed to form hemoglobin, an oxygen carrying protein inside red blood cells. Iron is also essential for proper cellular function i.e. energy metabolism, cell signaling, gene expression, and the regulation of cell growth and differentiation [3].

The term anemia denotes a reduction in the oxygen-carrying capacity of blood. In this condition in blood has a lower number of circulating red blood cells or a decrease in the hemoglobin concentration. Iron deficiency results from depletion of iron stores and occurs when iron absorption is insufficient compared to the metabolic iron demands. Two examples are depicted in **Figure 1**. The ratio between the iron absorbed and the amount ingested is typically low, but may range from 5% to 35% depending on circumstances and type of iron. A number of dietary factors influence iron absorption.

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Citation: Riccardi B, Paoli SDe, Resta S (2021) Comparison of Morphological Analysis of Two Different Products Based on Iron Pyrophosphate. J Nutraceuticals Food Sci Vol.6 No.6:34.

Treatment of iron deficiency

It is necessary to provide supplement for preventing iron loss, for correcting anaemia and replenishing body store. It has been known for a long time that although Iron is an essential element for the well-being of living organisms, its intake in humans represents a therapeutic challenge, for the numerous side effects that its administration produces, both oral and parenteral.

- **Oral iron supplementation:** The limits of iron supplementation are, low absorption, metallic flavor, gastrointestinal disturbances, nausea, constipation or diarrhea and oxidative stress
- **Intravenous supplementation:** Intravenous iron administration has a number of severe adverse reactions, and should be administered in a hospital environment under close supervision [4]

Evolution of Pharmacological Technology

Overcoming the disadvantages of oral and intravenous iron administration, technological research has provided us with effective and safe iron Delivery systems. Main Delivery systems used to improve iron absorption are described below and are

depicted in **Figure 2**.

Micronization

Micronization of pharmaceutical powders by using traditional technologies (jet milling) allows obtaining powders of particle size of the order of micrometers using the principle of micronic crushing by mechanical impact at very high dust speeds. This technology, however, does not allow the production of reproducible nanometric grain sizes (millionth of a millimeter), that is an aspect of the increasing interest in the pharmaceutical world today.

Microencapsulation

This technology consists in coating substances and nutrients with a membrane made of polymers of various natures, natural or synthetic. Polymers consist of proteins, polysaccharides, polyesters, phospholipids, etc.

Micro-encapsulation (understood as the preparation of both microcapsules and microspheres) can allow the change of color, shape, volume, solubility, reactivity, resistance, stability of the trapped substance.

The main applications of microencapsulation allow:

- Increasing the stability of a substance
- Overcoming of incompatibilities i.e. masking unpleasant odours and flavors

The sucrosom

The introduction of a new technology for Iron's carrier of called "Sucrosomial" [5] represents an evolution in the use of Sucrester, basic constituents of sucrosom that, which belong to the chemical species Emulsifiers used since 1936 as additives in many foods: ice cream, margarine, chocolate, mayonnaise, creamy saucer, etc.

Sucrester=E473 Sucrose esters of fatty acids

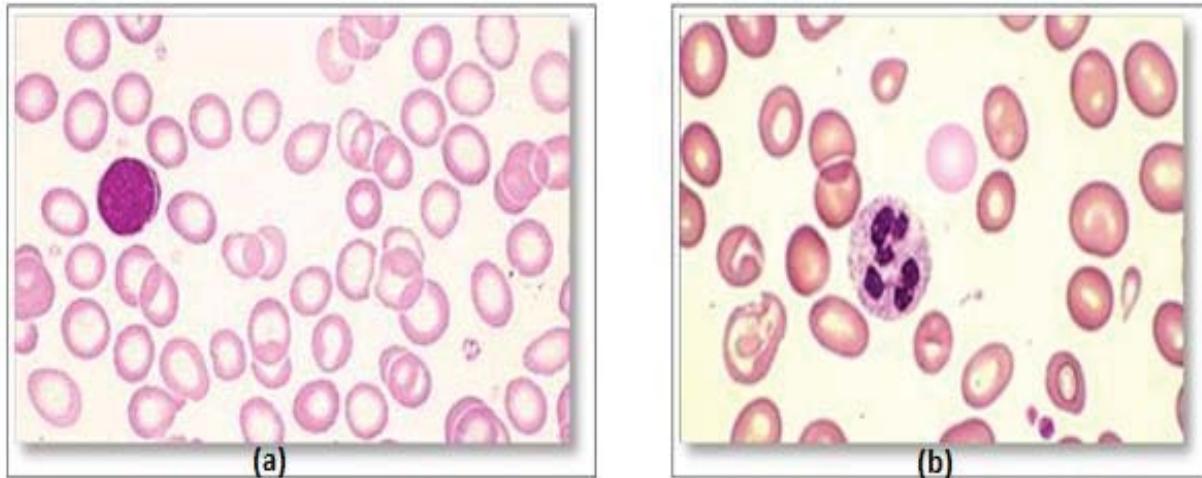


Figure 1 Anemia; (a): Iron deficiency anemia; (b): Megaloblastic anemia.

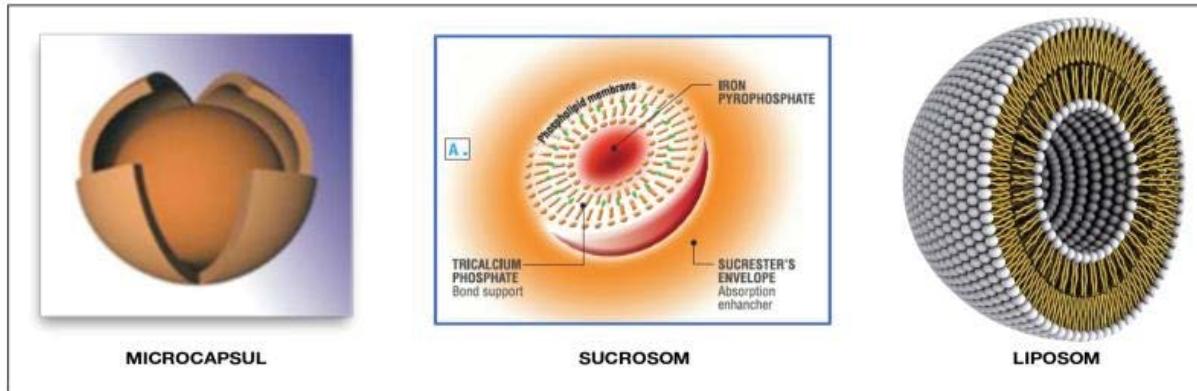


Figure 2 Schematic representation of the most popular delivery systems.

Liposomes

Nowadays the most widespread and used technology is represented by liposomes, for the ease of their production and versatility in their use. Liposomes consist of a double layer of phospholipids with an internal cavity that can contain and transport various substances in solution such as drugs or active substances.

Main Source of Iron for Supplements

Although the iron sulphate salt has the highest solubility and bioavailability [6-7]. It is however little used for food fortification because it is easily complex with food fibers and has a strong pro-oxidant effect, which reduces its bioavailability. For this reason the main source of iron used in Italy and in Europe is undoubtedly the lipofoods-lubrizol microencapsulated pyrophosphate iron named Lipofer. Available in dozens of brands from Companies and presented in various formulations is the most common form of iron supplement.

Chemical-Physical Characteristics of Lipofer

In all the official documents (Data sheets) and in the clinical works of lipofoods-lubrizol the lipofer is described as: "Micronized iron pyrophosphate coated with starch and lecithin" with all the chemical-physical characteristics that distinguish it. No morphological and/or granulometric of the liposomal form documentation of the product is provided [8-10]. For what reason all the Companies, without exception, that use the Lipofer, present it as "Pyrophosphate Iron in liposomes" falsifying the original distinctive characteristics of the product, without however providing morphological and structural evidence to support the claims. It is an unacceptable misinformation adopted to "ennoble" the properties of their products and pure marketing speculation, without any other added value. Liposomes are a

different technology, as well as improving the chemical-physical characteristics of substances that incorporate, significantly improve their bioavailability and tolerability [11-13]. For this reason they are widely used in the most demanding therapies, such as anticancer, antibiotics, vaccines, etc.

Comparison between Two Different Types of Pyrophosphate Iron

In this work we present the comparison between the lipofer of lipofoods-lubrizol and the pyrophosphate Iron produced by lipotech Argentina. Both the product are formed by iron pyrophosphate microencapsulated

The chemical and physical characteristics are described in the data sheet [14]. We have conducted morphological surveys of the products, at public and private institutions, specialized in this type of surveys, to evoke the characteristics of each. These are the results for lipotech's samples of microencapsulate pyrophosphate iron observed at the SEM **Figure 3**.

And for granulometric analysis **Figure 4** [14], the particle size distribution of sample were determined by laser diffraction method using Mastersizer 3000, Malvern Instruments UK.

And the results for lipofer's samples-sample material were observed using a scanning electron microscope DELPHI, solution all-in-one of **Correlative Light and Electronic Microscopy (CLEM)** **Figure 5** [15].

Comparison of iron concentration between microencapsulated pyrophosphate products

With the lipotech's microencapsulation technology, an iron concentration of 15% is obtained, [14] and the concentration is considerably higher than that of the other comparative salts, **Figure 6** and **Figure 7**.

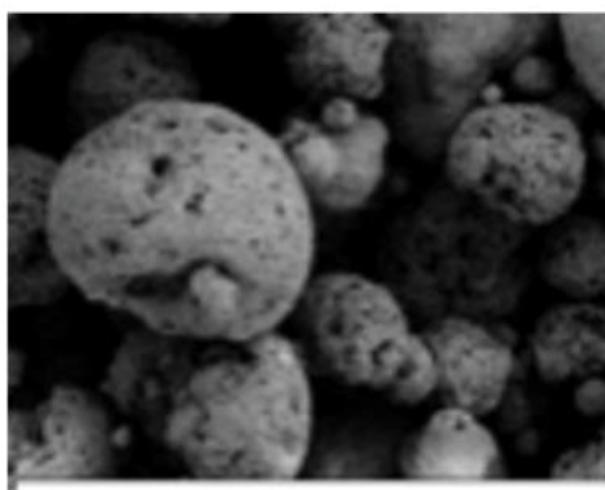
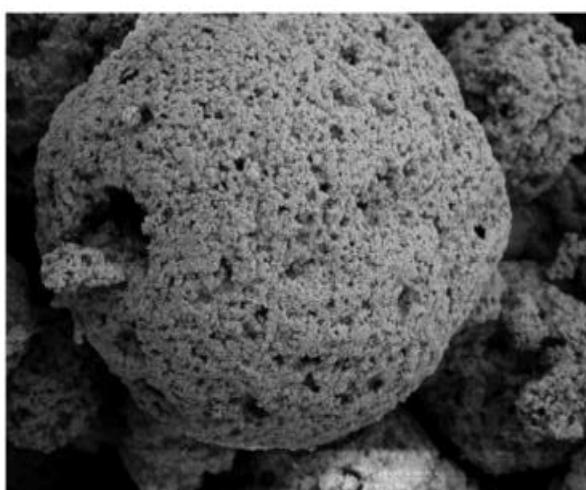


Figure 3: Samples of lipotech microencapsulate pyrophosphate iron observed at the Scanning Electron Microscope (SEM)-University of Salerno Italy.

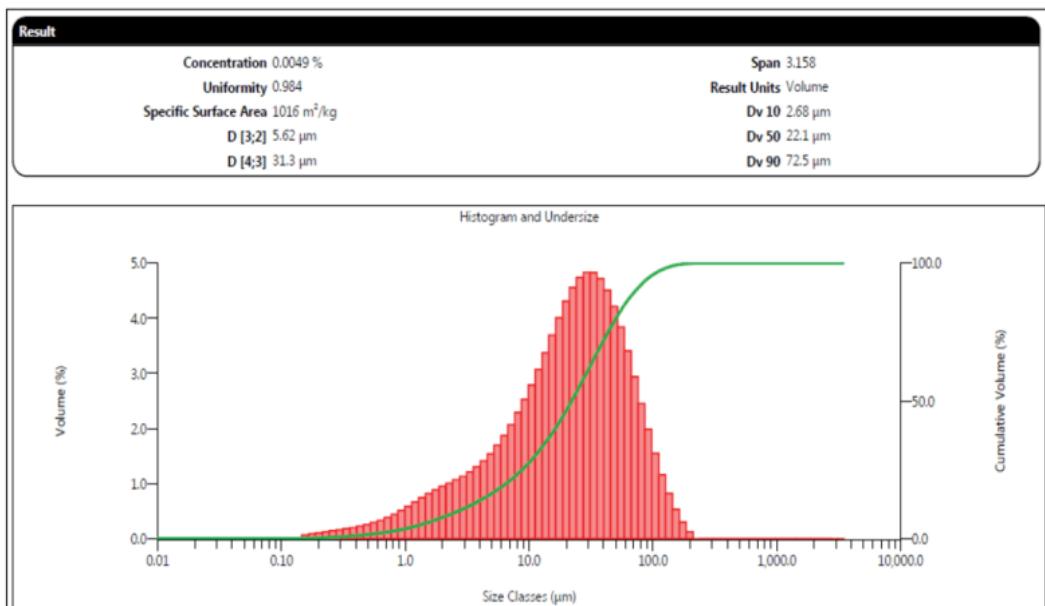


Figure 4: Granulometric analysis of samples of microencapsulated pyrophosphate iron lipotech-University of Salerno Italy.

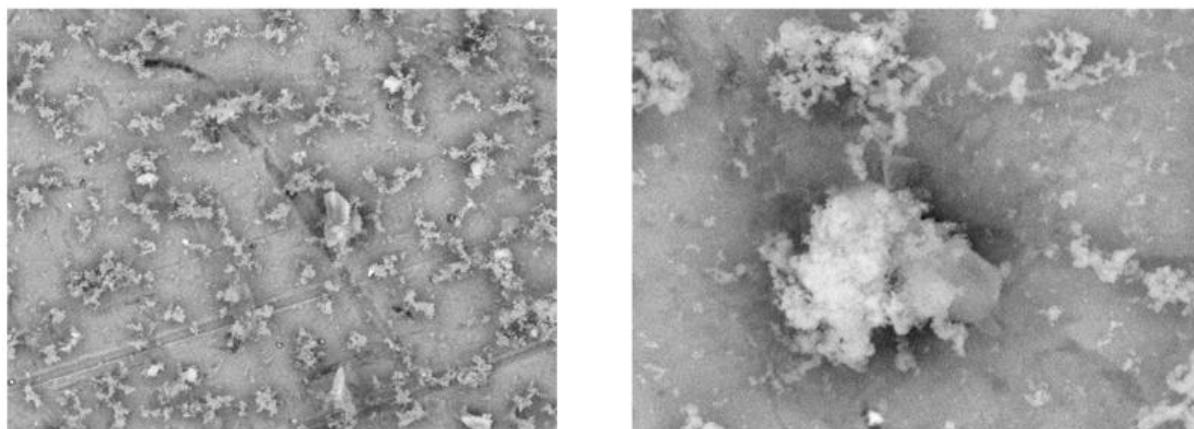


Figure 5: Sample of Iron pyrophosphate LIPOFER observed at the Scanning Electron Microscope [SEM] by Alfatest Milan –Italy.

The micro-encapsulation of Pyrophosphate Iron Lipotech

- *High titration of iron 15% ;*
- *Enhances bioavailability;*
- *Prevents organoleptic changes;*
- *Improves tolerability*

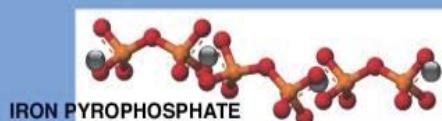


Figure 6: Properties of lipotech pyrophosphate iron.

COMPANY	PRODUCT	PERCENTAGE TITLE	TECHNOLOGY	REFERENCES
LIPOTECH	IRON PYROPHOSPHATE	Iron pyrophosphate 15%	Microincapsulation with phospholipids	Technical sheet
LIPOFOOD	LipoFer	Iron pyrophosphate 9%	Microincapsulation with starch and lecithin	Technical sheet
ALESCO	UltraFer	Iron pyrophosphate 10%	Microincapsulation with phospholipids Fatty acid matrix (sucrestere)	Technical sheet

Figure 7: Comparison of different types of microencapsulated iron pyrophosphate.

Conclusion

The comparison surveys we have conducted between lipotech's ferric pyrophosphate microencapsulated and iron pyrophosphate lipofer, show that first product iron is more concentrated than that present in lipofer, with the advantage of a lower cost.

With the technological treatment of the microencapsulation of lipotech, we get a product whose morphology and size is

similar to that of liposomes, contrary to what is observable for lipofer. This treatment could offer an up-grade of the already very good effectiveness and safety of the starting Iron Lipotech's product not encapsulated. This will be the goal of a future work.

Disclosure

The authors report no conflicts of interest in this work.

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