Challenges in the Development Process of Lipid Nanoemulsions for Parenteral Nutrition

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Lipid emulsions (ELP) used in parenteral nutrition represent a complex pharmaceutical formulation. These emulsions serve as vital sources of energy, essential fatty acids, and fat-soluble vitamins in nutritional therapy regimens. Therefore, following a systematic approach in the development process is crucial to ensure the safety of ELP. With this objective in mind, our study aimed to survey the stages involved in the development process of lipid nanoemulsions applied in parenteral nutrition and to identify the primary needs and challenges encountered throughout this process. Consequently, our analysis revealed 10 stages in the Product Development Process (PDP) and identified 20 specific needs that characterize the development of lipid nanoemulsions for parenteral nutrition. These identified needs offer valuable insights for future research endeavors to enhance the development of parenteral diets.

Keywords: Product Development. Parenteral Lipid Emulsions. Parenteral Nutrition. Quality Function Deployment (QFD).

Parenteral Nutrition (PN) involves the intravenous infusion of nutrients, comprising a solution or emulsion containing macronutrients and micronutrients. The primary goal of PN is to synthesize or maintain tissues, organs, and systems [1]. Within PN, fatty acids (FA) are delivered through parenteral lipid emulsions (ELP). These emulsions consist of essential fatty acids (AGE), phospholipids, and fat-soluble vitamins and employ a complex nanotechnological delivery system. Additionally, ELP is a high-density energy source and varies in the quantity, type, and source of fatty acids [2,3].

PN is designed to fulfill patients' nutritional and metabolic requirements. Consequently, ELP plays a crucial role in patient prognosis due to its significant impact on the immune and inflammatory systems. While PN represents a costly therapeutic approach, when appropriately indicated and administered, ELP can mitigate complications, reduce hospitalization duration, and decrease overall medical care costs [4].

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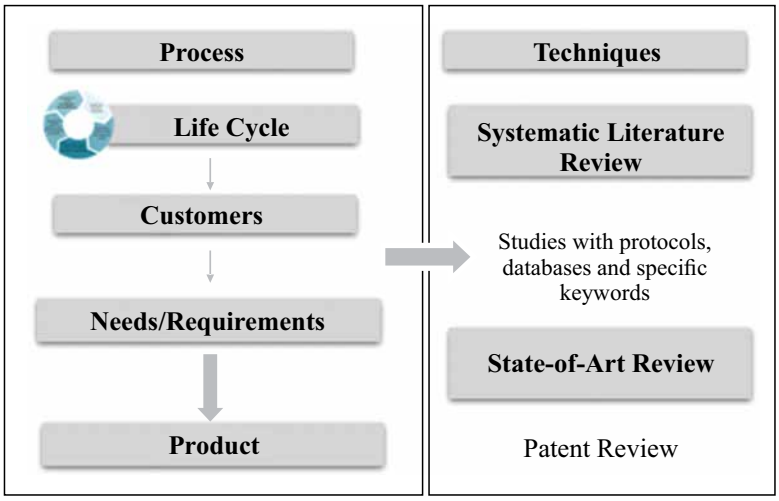
ELP is configured as a pharmaceutical product, necessitating adherence to a meticulous development process to ensure its safety. Given the complexity of the ELP development process, characterized by the vast amount of information involved, careful navigation is crucial. Notably, many design tools are applicable in the early stages of development. The selection of methodologies and technologies employed in ELP development is paramount, as they dictate the characteristics of the final product [5,6]. Therefore, this study aims to survey the stages involved in executing the ELP development process, specifically focusing on lipid nanoemulsions applied in parenteral nutrition, and to identify the primary needs and challenges encountered.

Materials and Methods

This study employs a quantitative approach to explore scientific and technological aspects. The methodology follows an applied framework, adhering to the stages of lipid nanoemulsion development for parenteral nutrition as proposed by De Paula (2004) [7]. De Paula's model integrates management principles and product development techniques [6]. A schematic representation of the methodological process and techniques employed (Figure 1).

Figure 1. Research process and techniques.



Initially, a comprehensive analysis was conducted to map current and future processes and the needs and contextual factors pertinent to the development of lipid nanoemulsions for parenteral nutrition therapy. It involved identifying and systematizing the stages and processes throughout the life cycle and articulating the discerned needs.

Results and Discussion

The steps in the development process were identified by adapting Yugue's (2009) drug development processes [8]. A detailed review mapped out 20 distinct needs that characterize the process of developing lipid nanoemulsions for parenteral nutrition (Table 1).

Amaral and colleagues (2017) [6] emphasize the significance of identifying needs in product development, as products should be designed based on these needs. This approach provides a comprehensive understanding of the design objectives.

Parenteral lipid emulsions play a crucial role in clinical practice and patient prognosis [9], and they are becoming an increasingly important area of research. The process of developing lipid nanoemulsions for parenteral nutrition follows well-defined steps. It is worth noting that inadequate adherence to any of these stages may compromise the Product Development Process (PDP) outcomes. Regarding challenges, it is pertinent to highlight the necessity of importing inputs/raw materials for the production process and the absence of domestic companies manufacturing these products in Brazil. Brazil has limited influence in this technology and lacks significant knowledge appropriation in this sector, leading to external dependence and substantial costs for the country.

However, the absence of domestic companies specializing in developing lipid nanoemulsions for parenteral nutrition could present an opportunity. Nonetheless, realizing this potential requires proactive economic measures to stimulate technical, scientific, and technological advancements in this field.

Conclusion

The identified needs are essential for developing lipid nanoemulsions applied in parenteral nutrition. Moreover, these needs can serve as valuable contributions to studies to formulate parenteral diets in future research endeavors. Other researchers should undertake the development of a reference model for designing and developing parenteral diets, which could provide support for both future research and industry applications.

Table 1. Steps and needs in developing lipid nanoemulsions applied in parenteral nutrition.

Stages	Stages of PDP	Requisites
1	Concept study	Medical viability
		Regulatory viability
		Development feasibility
		Manufacturing feasibility
		Low production cost
		Commercial feasibility
2	Pre-clinical study	Complying with published literature
3	Method development (raw material)	Viable raw material cost
4	Method validation (raw material)	Potential raw material
5	Pre-formulation study	Chemical stable raw material/inputs
		Inputs with low degradation capacity
6	Product/formulation development	Production feasibility
7	Development of analytical method (finished product)	Precise, consistent, and reliable data
8	Stability study	Accelerated stability
		Long-term stability
9	Clinical study	Be safe
		Complying with ANVISA requirements
10	Product registration dossier/report	Meeting published scientific needs
		Be viable for regulatory approval
		Complying with criteria for product approval and price officialization

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