Commentary
Volume 14:05, 2024

Journal of Bioprocessing & Biotechniques

ISSN: 2155-9821 Open Access

Strategies to Improve Solubility and Bioavailability of Lipophilic Drugs: Focusing on Fenretinide

Rodrigo Jun*

Department of Biological Engineering, Inha University, Michuhol-gu, Republic of Korea

Introduction

The challenge of improving the solubility and bioavailability of lipophilic drugs is a significant issue in pharmaceutical development. Many therapeutic compounds, particularly those that are hydrophobic, exhibit poor solubility in aqueous environments, leading to limited absorption in the gastrointestinal tract and reduced efficacy. This problem is especially pertinent in the case of drugs like fenretinide, a synthetic derivative of retinoic acid, which has shown promise in treating cancer, skin disorders, and other health conditions. However, its clinical utility has been hindered by its poor solubility and bioavailability. To address these challenges, several strategies have been developed over the years to enhance the solubility, stability, and absorption of lipophilic drugs, with a particular focus on fenretinide. Fenretinide, also known as N-(4-hydroxyphenyl) retinamide, is a potent retinoid that has demonstrated anticancer properties, including the ability to induce apoptosis and inhibit tumor growth. Despite its promising therapeutic effects, fenretinide's poor water solubility limits its absorption and bioavailability when administered orally. As a result, significant efforts have been made to improve the delivery of fenretinide to enhance its therapeutic potential. Various strategies have been explored to overcome the solubility and bioavailability challenges of lipophilic drugs like fenretinide, including formulation approaches, molecular modifications, and the use of drug delivery systems.

Description

One of the most common strategies to improve the solubility of lipophilic drugs is through the use of solubilizing agents. These agents can help increase the apparent solubility of the drug in aqueous solutions, facilitating its absorption in the gastrointestinal tract. In the case of fenretinide, several solubilizing agents have been tested, including surfactants, co-solvents, and cyclodextrins. Surfactants such as polysorbates and bile salts are often used to enhance the solubility of lipophilic compounds by reducing surface tension and promoting the formation of micelles that can solvate the drug molecules. Cyclodextrins, which are cyclic oligosaccharides, are particularly useful in forming inclusion complexes with hydrophobic drugs like fenretinide, improving their solubility in water. These complexes can increase the drug's aqueous solubility, stability, and even its permeability across biological membranes, improving its bioavailability. Another approach to enhance the bioavailability of fenretinide is through the use of lipid-based drug delivery systems, such as liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs). These lipid-based carriers can encapsulate lipophilic drugs like fenretinide, improving their solubility and protecting them from degradation. Liposomes, which are vesicular systems made from phospholipids, are particularly effective at encapsulating hydrophobic drugs. These carriers can improve drug stability, control drug release, and increase the drug's half-life in circulation, all of which contribute to enhanced bioavailability [1].

Similarly, SLNs and NLCs offer advantages in terms of drug stability and controlled release. These systems are composed of solid or liquid lipids that provide a matrix for the drug, allowing for sustained and targeted drug release. Lipid-based carriers also enhance drug uptake in the gastrointestinal tract by improving the drug's solubility and facilitating its transport across cell membranes. Nanotechnology has also emerged as a promising strategy to improve the solubility and bioavailability of fenretinide. Nanoparticles, particularly those made of biocompatible materials such as poly(lactic-co-glycolic acid) (PLGA), are often used to encapsulate lipophilic drugs, enhancing their solubility and stability. The small size of nanoparticles allows for increased surface area, which can improve drug dissolution rates and enhance drug absorption. Furthermore, nanoparticles can be engineered to target specific tissues or cells, improving the therapeutic efficacy of the drug. In the case of fenretinide, nanoparticles have been designed to improve its delivery to target sites, such as cancer cells, where it can exert its anticancer effects more efficiently. Targeted nanoparticles also reduce the risk of systemic side effects, as they allow for more precise drug delivery to the intended site of action. In addition to these drug delivery strategies, the chemical modification of fenretinide itself has been explored to improve its solubility and bioavailability. For example, the development of prodrugs—chemically modified versions of fenretinide that can be metabolized into the active drug once inside the body—has been proposed as a strategy to overcome solubility issues. Prodrugs can be designed to have enhanced solubility and permeability, which improves their absorption in the gastrointestinal tract. Once absorbed, the prodrug is converted into the active form of fenretinide, which can then exert its therapeutic effects. This approach has been successfully used with other lipophilic drugs, and it holds potential for improving the clinical use of fenretinide [2,3].

Formulation approaches also play a crucial role in enhancing the bioavailability of lipophilic drugs like fenretinide. Solid dispersions, for example, are one formulation technique that has been used to improve the solubility of poorly water-soluble drugs. In solid dispersions, the drug is dispersed in a hydrophilic matrix, which increases its surface area and enhances its dissolution rate. This technique has been applied to fenretinide to improve its solubility and bioavailability. Other formulation strategies include the use of micronization, in which the drug is reduced to a fine powder to increase its surface area and improve its dissolution, and the use of hydrophilic polymers that can enhance the dissolution and solubility of the drug. The choice of the route of administration can also impact the bioavailability of fenretinide. While oral administration is the most common route for drug delivery, it may not always be the most effective for lipophilic drugs. For drugs with poor solubility and absorption in the gastrointestinal tract, alternative routes such as intravenous (IV) administration may be considered. However, IV administration is not always ideal due to the inconvenience and cost associated with it. Thus, improving the oral bioavailability of fenretinide remains a priority. By utilizing the aforementioned strategies, the goal is to achieve higher concentrations of the drug in the bloodstream following oral administration, improving its therapeutic efficacy and reducing the need for more invasive administration routes. Despite the promising strategies to improve the solubility and bioavailability of fenretinide, challenges remain in optimizing these approaches for clinical use. The process of formulation development involves careful consideration of factors such as drug stability, release kinetics, and the potential for side effects. Each strategy must be evaluated for its ability to provide a balance between solubility, bioavailability, and safety. Furthermore, the large-scale production of formulations such as

***Address for Correspondence:** Rodrigo Jun, Department of Biological Engineering, Inha University, Michuhol-gu, Republic of Korea, E-mail: rorrigojun@gmail.com*

Received: 02 September, 2024, Manuscript No. Jbpbt-24-153235; **Editor Assigned:** 04 September, 2024, PreQC No. P-153235; **Reviewed:** 17 September, 2024, QC No. Q-153235; **Revised:** 23 September, 2024, Manuscript No. R-153235; **Published:** 30 September, 2024, DOI: 10.37421/2155-9821.2024.14.637

liposomes or nanoparticles requires specialized equipment and may present scalability challenges. Additionally, the regulatory approval of novel drug formulations can be a lengthy and complex process, requiring extensive preclinical and clinical testing to demonstrate safety and efficacy [4,5].

Conclusion

Enhancing the solubility and bioavailability of lipophilic drugs like fenretinide is essential to maximizing their therapeutic potential. The strategies explored—ranging from the use of solubilizing agents and lipid-based carriers to chemical modifications and novel drug delivery systems—hold great promise in improving the clinical efficacy of fenretinide and other hydrophobic compounds. Through continued research and development, these approaches can lead to the creation of more effective formulations that increase the accessibility and effectiveness of fenretinide for treating conditions such as cancer, skin disorders, and potentially other diseases. As we move forward, the integration of these strategies into clinical practice will require careful optimization, but the potential benefits for patient outcomes are substantial.

Acknowledgement

None.

Conflict of Interest

None.

References

1. Lobo, Sonia. "Is there enough focus on lipophilicity in drug discovery?." *Expert Opin Drug Discov* 15 (2020): 261-263.
2. Veber, Daniel F., Stephen R. Johnson, Hung-Yuan Cheng and Brian R. Smith, et al. "Molecular properties that influence the oral bioavailability of drug candidates." *J Med Chem* 45 (2002): 2615-2623.
3. Khalil, Samar, Tara Bardawil, Carla Stephan and Nadine Darwiche, et al. "Retinoids: A journey from the molecular structures and mechanisms of action to clinical uses in dermatology and adverse effects." *J Dermatol Treat* 28 (2017): 684-696.
4. Batra, Sandeep, C. Patrick Reynolds and Barry J. Maurer. "Fenretinide cytotoxicity for Ewing's sarcoma and primitive neuroectodermal tumor cell lines is decreased by hypoxia and synergistically enhanced by ceramide modulators." *Cancer Res* 64 (2004): 5415-5424.
5. Song, Michael M., Monish R. Makena, Ashly Hindle and Balakrishna Koneru, et al. "Cytotoxicity and molecular activity of fenretinide and metabolites in T-cell lymphoid malignancy, neuroblastoma, and ovarian cancer cell lines in physiological hypoxia." *Anti-Cancer Drugs* 30 (2019): 117-127.

How to cite this article: Jun, Rodrigo. "Strategies to Improve Solubility and Bioavailability of Lipophilic Drugs: Focusing on Fenretinide." *J Bioprocess Biotech* 14 (2024): 637.