Micro Nano Bio Aspects

https://www.mnba-journal.com

Online ISSN: 2980-8081

Main distinctions between tocosome and nano-liposome as drug delivery systems: A scientific and technical point of view

M. R. Mozafari[1*] and Mehran Alavi[2,3]

[1]*Australasian Nanoscience and Nanotechnology Initiative (ANNI), 8054 Monash University LPO, Clayton, Victoria 3168, Australia*

[2]*Department of Biological Science, Faculty of Science, University of Kurdistan, Sanandaj, Kurdistan, Iran*

[3]*Nanobiotechnology Department, Faculty of Innovative Science and Technology, Razi University, Kermanshah, Iran*

ARTICLE INFO

Letter to the editor

Article history:
Received: 22 Feb 2023
Revised: 10 Mar 2023
Accepted: 12 Mar 2023
ePublished: 12 Mar 2023

Keywords:
Alpha tocopherol, Tocosome, Liposome, Nanoliposome, Drug delivery, Encapsulation

ABSTRACT

Some of the currently available encapsulation systems, including liposomes, nanoliposomes, and solid lipid nanoparticles, have already been approved to be used in the pharmaceutical, food, textile, and cosmetic markets. These systems have proven to be useful for the encapsulation, controlled release, targeting drugs, vaccines (including Covid-19 vaccines), and other bioactive compounds in vitro and in vivo. The most recently invented encapsulation system, known as "tocosome", is formulated employing two derivatives of alpha-tocopherol (vitamin E). Although tocosomes are somehow similar to lipid vesicles, they possess exceptional characteristics mainly due to the presence of unique ingredients in their structures. There have been ambiguities in the scientific literature regarding the differences between tocosomes, liposomes, and nanoliposomes. The present article aims to provide brief scientific explanations in a clear way to highlight differences between the mentioned drug carriers.

DOI: https://doi.org/10.22034/mnba.2023.386877.1023

Dear editor,

Efficient delivery of therapeutic agents via different routes of drug administration requires biodegradable, non-toxic, adequately stable and targetable encapsulation systems [1, 2]. Among the food and drug administration (FDA)-approved drug delivery systems, liposomes, and their nanometric version (nanoliposomes) are leading the pharmaceutical market [3-5]. Presented to the scientific community in 1960's, liposomes and nanoliposomes are considered to be the most established and well-studied drug carrier technologies [6]. On the other hand, tocosome, a novel vesicular system for drug encapsulation and targeting, was first introduced in the year 2017 by Mozafari et al. [7]. This team manufactured a tocosomal formulation for the encapsulation and controlled release of an anticancer drug, i.e., 5-fluorouracil (5-FU). The tocosomal formulation showed long-term stability and ideal drug release properties.

One of the main characteristics of tocosomes is their ingredient molecules, which make them unique and distinguished from other drug carrier systems [8]. These ingredients are two phosphorylated forms of vitamin E derivatives, α-tocopheryl phosphate (TP) and di-α-tocopheryl phosphate (T_2P) (Figure 1). Tocosomes are mainly spherical, closed, continuous bilayer vesicles composed of one or multiple bilayer membranes (in which case they are classified as a unilamellar vesicle or multilamellar vesicle respectably). Presence of TP and T_2P molecules differentiates tocosomes from other drug carrier systems such as liposomes, nanoliposomes, solid lipid nanoparticles (SLN), and vesicular phospholipid gels [9]. These two ingredients have several proven health-benefit properties such as atherosclerosis-preventive, as well as anti-inflammatory and cardioprotective effects and they are extremely strong antioxidants [10]. There are ambiguities regarding the classification of TP and T_2P molecules and in some articles, they are referred to as phospholipids inaccurately. It should be noted that, in their chemical structures, both TP and T_2P molecules lack glycerol linker and fatty acid tails

*Corresponding author. E-mail: dr.m.r.mozafari@gmail.com

which are crucial components of a phospholipid molecule. These tocopherol derivatives include a chroman head (with two rings: one heterocyclic and one phenolic) and one or two phytyl tail(s). While TP molecule has only one tail (similar to a surfactant molecule), T_2P molecule possesses two phytyl tails. However, phospholipid molecules possess two fatty acid tails with or without double bonds. The only similarity between TP, T_2P, and phospholipids is the presence of a phosphate group in their structure. Consequently, they possess amphiphilic properties and can form stable bilayer vesicles that can encapsulate hydrophilic, hydrophobic and amphiphilic compounds [11].

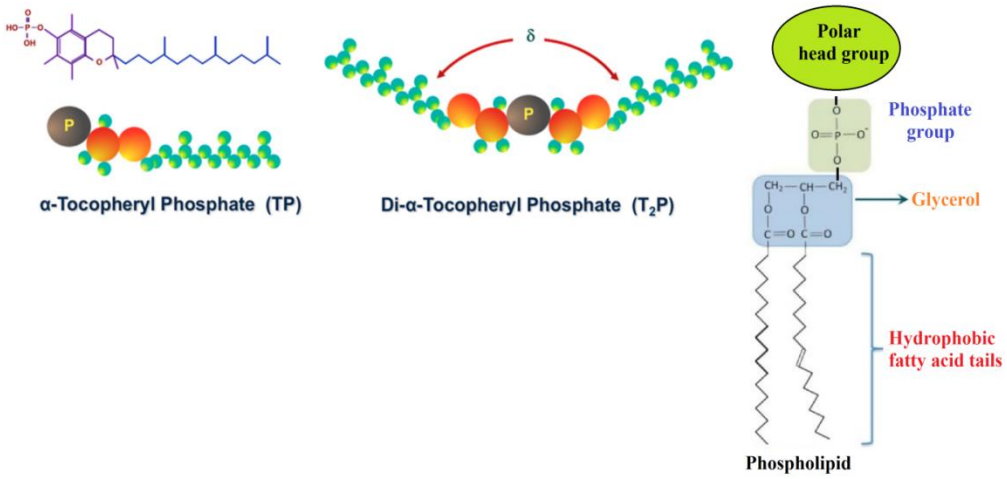

Fig 1. Chemical structures of α-tocopheryl phosphate (TP), di-α-tocopheryl phosphate (T_2P), and a phospholipid molecule (adopted and modified from [11]).

Different procedures can be used for the manufacture of tocosomes in small or large scales. These include conventional techniques (e.g., thin-layer hydration, ethanol injection, homogenization, microfluidization, sonication, and freeze-dry methods) or novel and patented techniques such as Mozafari method, which is a green and scalable method [12, 13]. In a recent publication, Razmimanesh and colleagues used Mozafari method for the preparation of nanocarriers that they erroneously called "tocosome" [14]. The article describes the manufacture of the nanocarriers "without employing T_2P molecules". This is while T_2P is an essential ingredient of tocosomal drug carriers due to the presence of which tocosome has its own stability and skin-penetration properties different than other vesicular drug carriers. This fundamental ingredient is not mentioned in the article at all and in the methods section, authors describe the preparation of the nanocarriers using TP, cholesterol, polyethylene glycol (PEG), different types of phospholipids (e.g., phosphatidylcholine (PC), distearoyl phosphatidylcholine (DSPC), and 1,2-Distearoylphosphatidylethanolamine (DSPE)), and stearylamine (SA) [14]. It is obvious that the formulated nanocarriers are nanoliposomes with added TP as an antioxidant (stabilizing agent) and not tocosomes, which strictly require the presence of both TP and T_2P molecules, as main ingredients, in their bilayer structures. It is hoped that the present article was able to shed light on the differences between tocosomes, liposomes, and nanoliposomes. It should be seriously noted that each of these drug carrier technologies is designed and used for different applications based on its properties.

Study Highlights

- Tocosome is a novel drug delivery system which can be used for the encapsulation of different bioactive compounds.
- The main ingredients of tocosome are alpha-tocopheryl phosphate (TP) and di-alpha-tocopheryl phosphate (T_2P).
- Different procedures, such as Mozafari method, can be used for the manufacture of tocosomes in small or large scales.
- The mentioned method does not require utilization of toxic solvents, detergents or harsh procedures for the manufacture of carrier systems.

- The tocosomal formulation prepared using Mozafari method showed long-term stability and ideal drug release properties.

Abbreviations

5-FU: 5-fluorouracil
DSPC: Distearoylphosphatidylcholine
DSPE: 1,2-Distearoylphosphatidylethanolamine
FDA: Food and drug administration
PC: Phosphatidylcholine
PEG: Polyethylene glycol
SA: Stearylamine
SLN: Solid lipid nanoparticles
T_2P: di-α-tocopheryl phosphate
TP: α-tocopheryl phosphate

Funding

This work was not supported by any institutes.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

This article does not contain any studies with animals or human participants performed by any of the authors.

Authors' contribution

Both authors: conceptualization, preparing the first draft, and revising the manuscript.

Acknowledgments

Declared none.

References

1. Alavi M, Hamblin MR, Martinez F, Aghaie E, Khan H, Menezes IA. Micro and nanoformulations of insulin: new approaches. Nano Micro Biosystems. 2022;1(1):1-7. doi:https://doi.org/10.22034/nmbj.2022.157284
2. Adefegha SA, Salawi A, Bumrungpert A, Khorasani S, Torkaman S, Mozafari MR, et al. Encapsulation of polyphenolic compounds for health promotion and disease prevention: Challenges and opportunities. Nano Micro Biosystems. 2023;1(2):1-12. doi:https://doi.org/10.22034/nmbj.2023.163756
3. Al Badri YN, Chaw CS, Elkordy AA. Insights into Asymmetric Liposomes as a Potential Intervention for Drug Delivery Including Pulmonary Nanotherapeutics. Pharmaceutics. 2023;15(1):294. doi:https://doi.org/10.3390/pharmaceutics15010294
4. Song J-W, Liu Y-S, Guo Y-R, Zhong W-X, Guo Y-P, Guo L. Nano–Liposomes Double Loaded with Curcumin and Tetrandrine: Preparation, Characterization, Hepatotoxicity and Anti–Tumor Effects. International Journal of Molecular Sciences. 2022;23(12):6858. doi:https://doi.org/10.3390/ijms23126858
5. Emtiazi H, Salari Sharif A, Hemati M, Fatemeh Haghiralsadat B, Pardakhti A. Comparative Study of Nano-liposome and Nano-niosome for Delivery of Achillea Millefolium Essential Oils: Development, Optimization, Characterization and Their Cytotoxicity Effects on Cancer Cell Lines and Antibacterial Activity. Chemistry & Biodiversity. 2022;19(10):e202200397. doi:https://doi.org/10.1002/cbdv.202200397
6. Nsairat H, Khater D, Sayed U, Odeh F, Al Bawab A, Alshaer W. Liposomes: structure, composition, types, and clinical applications. Heliyon. 2022;8(5):e09394. doi:https://doi.org/10.1016/j.heliyon.2022.e09394
7. Mozafari MR, Javanmard R, Raji M. Tocosome: Novel drug delivery system containing phospholipids and tocopheryl phosphates. International Journal of Pharmaceutics. 2017;528(1):381-2. doi:https://doi.org/10.1016/j.ijpharm.2017.06.037
8. Shahgholian N. Encapsulation and Delivery of Nutraceuticals and Bioactive Compounds by Nanoliposomes and Tocosomes as Promising Nanocarriers. Handbook of Nutraceuticals and Natural Products2022. p. 403-39. doi:https://doi.org/10.1002/9781119746843.ch17
9. Kabarkouhi Z, Mehrarya M, Gharehchelou B, Jalilian Z, Jalili R, Wintrasiri MN, et al. Liposome, Nanoliposome and Allied Technologies in Covid-19 Vaccines: Key Roles and Functionalities. Curr Drug Deliv. 2022;20(1):3-7. doi:https://doi.org/10.2174/1567201819666220427125342
10. Raoufi E, Bahramimeimandi B, Salehi-Shadkami M, Chaosri P, Mozafari MR. Methodical Design of Viral Vaccines Based on Avant-Garde Nanocarriers: A Multi-Domain Narrative Review. Biomedicines. 2021;9(5):520. doi:https://doi.org/10.3390/biomedicines9050520
11. Zarrabi A, Alipoor Amro Abadi M, Khorasani S, Mohammadabadi M-R, Jamshidi A, Torkaman S, et al. Nanoliposomes and Tocosomes as Multifunctional Nanocarriers for the Encapsulation of Nutraceutical and Dietary Molecules. Molecules. 2020;25(3):638. doi:https://doi.org/10.3390/molecules25030638
12. Alavi M, Mozafari MR, Hamblin MR, Hamidi M, Hajimolaali M, Katouzian I. Industrial-scale methods for the manufacture of liposomes and nanoliposomes: pharmaceutical, cosmetic, and nutraceutical aspects. Micro Nano Bio Aspects. 2022;1(2):26-35.

doi:https://doi.org/10.22034/mnba.2022.159371
13. Alavi M, Rai M, Varma RS, Hamidi M, Mozafari MR. Conventional and novel methods for the preparation of micro and nanoliposomes. Micro Nano Bio Aspects. 2022;1(1):18-29. doi:https://doi.org/10.22034/mnba.2022.150564
14. Razmimanesh F, Sodeifian G. Investigation of Temperature-Responsive Tocosomal Nanocarriers as the Efficient and Robust Drug Delivery System for Sunitinib Malate Anti-Cancer Drug: Effects of MW and Chain Length of PNIPAAm on LCST and Dissolution Rate. Journal of Pharmaceutical Sciences. 2022;111(7):1937-51. doi:https://doi.org/10.1016/j.xphs.2021.12.022

HOW TO CITE THIS ARTICLE:
Mozafari MR, Alavi M. Main distinctions between tocosome and nano-liposome as drug delivery systems: A scientific and technical point of view. Micro Nano Bio Aspects. 2022; 2(1): 26-29.
doi: https://doi.org/10.22034/mnba.2023.386877.1023