Available online on 15.08.2026 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Research Article

Comparative *In Vitro* Release Study of Vitamin C from Spirulina-Based Matrix Tablets: Influence of Excipients on Dissolution Kinetics and Tablet Performance

Assogba Gabin Assanhou [1*], Paul Boucari [1,2], Parfait Doffon [1,2], Urbain Comlan Kassehin [1,2], Virgile Ahyi [3], Fernand A Gbaguidi [4]

[1] Unité de Recherche en Pharmacie Galénique et de Technologie Pharmaceutique, UFR Pharmacie, Centre de Recherche et de Développement du Médicament PharmaLab, Ecole Doctorale des Sciences de la Santé, Faculté des Sciences de la Santé, Université d'Abomey-Calavi, Campus du champ de Foire, 01BP 188, Cotonou, Bénin.

[2] Unité de Recherche en Chimie Analytique et d'Analyse des Médicaments, UFR Pharmacie, Centre de Recherche et de Développement du Médicament PharmaLab, Ecole Doctorale des Sciences de la Santé, Faculté des Sciences de la Santé, Université d'Abomey-Calavi, Campus du champ de Foire, 01BP 188, Cotonou, Bénin.

[3] Inter-Regional University of Industrial Engineering Biotechnologies and Applied Sciences, Unité de formation en Ingénierie des Procédés de Production, Laboratoire de Pharmacologie et Toxicologie, 07BP231 Cotonou-BENIN.

[4] Unité de Recherche en Chimie Organique et Pharmaceutique, UFR Pharmacie, Centre de Recherche et de Développement du Médicament PharmaLab, Ecole Doctorale des Sciences de la Santé, Faculté des Sciences de la Santé, Université d'Abomey-Calavi, Campus du champ de Foire, 01BP 188, Cotonou, Bénin.

Article Info:

Article History:

Received 10 May 2026
Reviewed 27 June 2026
Accepted 18 July 2026
Published 15 August 2026

Cite this article as:

Assanhou AG, Boucari P, Doffon P, Kassehin UC, Ahyi V, Gbaguidi FA, Comparative *In Vitro* Release Study of Vitamin C from Spirulina-Based Matrix Tablets: Influence of Excipients on Dissolution Kinetics and Tablet Performance, Journal of Drug Delivery and Therapeutics. 2026; 16(8):33-38 *DOI: https://doi.org/10.22270/jddt.v16i8.7902*

For Correspondence:

Assogba Gabin ASSANHOU, Unité de Recherche en Pharmacie Galénique et de Technologie Pharmaceutique, UFR Pharmacie, Centre de Recherche et de Développement du Médicament PharmaLab, Ecole Doctorale des Sciences de la Santé, Faculté des Sciences de la Santé, Université d'Abomey-Calavi, Campus du champ de Foire, 01BP 188, Cotonou, Bénin.

Abstract

Objective (s): This study aimed to compare the *in vitro* release kinetics of vitamin C from spirulina-based matrix tablets and to evaluate the influence of selected excipients on dissolution behavior and tablet performance.

Design: Four formulations were prepared by varying the proportions of vitamin C, spirulina, HPMC, starch, microcrystalline cellulose, and lactose. Tablets were manufactured by direct compression and evaluated according to pharmacopeial standards.

Intervention (s): Dissolution testing was performed in 0.1 N HCl (pH 1.2) at 37 °C for 4 hours. Vitamin C quantification was carried out by HPLC DAD at 245 nm.

Main outcome measure(s): Dissolution profiles, mechanical properties, and similarity/difference factors (f_2, f_1).

Results: Spirulina significantly improved tablet hardness, while starch and microcrystalline cellulose accelerated vitamin C release. HPMC produced a sustained release matrix, whereas lactose exerted a neutral to slightly inhibitory effect. Spirulina containing tablets showed prolonged release but also partial vitamin C oxidation after 90 minutes, likely due to transition metal ions naturally present in spirulina. Dissolution comparison revealed non similarity between formulations (e.g., F2 vs F4: f_1 = 17.2; F3 vs F4: f_2 = 42.75).

Conclusion: Excipient composition strongly modulates both mechanical strength and release kinetics of vitamin C matrix tablets. Spirulina enhances hardness and sustains release but may promote oxidative degradation. Optimizing excipient ratios is essential for achieving robust and stable nutraceutical formulations. In vivo studies are recommended.

Keywords: Spirulina; Vitamin C; Matrix tablets; Dissolution; Excipients

1. INTRODUCTION

The global market for dietary supplements has experienced sustained growth over the past decade, reaching nearly USD 180 billion in 2024 and projected to exceed USD 250 billion by 2029, with an estimated annual growth rate of 7.6% [1]. Unlike conventional medicines, which are subject to stringent regulatory requirements and substantial research and development costs, dietary supplements benefit from comparatively flexible regulatory frameworks and lower production

expenses [2]. Their widespread availability in pharmacies, supermarkets, and online platforms, combined with intensive marketing strategies and strong consumer demand, has contributed to their increasing use across all age groups. These products are generally intended to complement a balanced diet and support physiological functions, including immune defense, cardiovascular health, musculoskeletal integrity, and digestive well-being [3].

Among the most widely consumed nutraceuticals, vitamin C (ascorbic acid) occupies a prominent position. Its popularity increased markedly during and after the COVID-19 pandemic, owing to its well-documented antioxidant, immunostimulatory, and anti-aging properties. Vitamin C plays a pivotal role in collagen synthesis, wound healing, regeneration of other antioxidants, and modulation of immune responses. It has also been associated with beneficial effects in cardiovascular prevention and certain neurodegenerative disorders [5,6]. However, its intestinal absorption is dose-dependent and limited by saturable transport mechanisms, underscoring the importance of appropriate formulation strategies to optimize its bioavailability [4].

Spirulina (*Arthrospira platensis*), a cyanobacterium widely consumed as a dietary supplement, is often described as a "superfood" due to its exceptionally high protein content (up to 70% of dry weight), essential amino acids, iron, and diverse micronutrients. It is classified by the U.S. Food and Drug Administration as Generally Recognized As Safe (GRAS) and has demonstrated immunomodulatory and nutritional benefits in both clinical and public health contexts [7]. Nevertheless, spirulina contains negligible amounts of vitamin C, which may limit its overall antioxidant capacity [8]. The combination of spirulina with vitamin C within a single formulation therefore represents a promising strategy to enhance nutritional value and exploit potential synergistic effects.

Pharmaceutical technology provides several approaches for modulating the release of active compounds. Matrix tablets, particularly those based on hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC), are well suited for sustained-release formulations. By incorporating the active ingredient within a polymeric matrix, these systems enable controlled drug release over time, thereby reducing dosing frequency and improving patient adherence. Previous work by Marie Miguel *et al.,* (2023) reported the successful development of spirulina–vitamin C matrix tablets that met most pharmacopeial quality requirements, although insufficient hardness was observed, indicating the need for further optimization [9].

The present study was therefore designed to compare the *in vitro* release profiles of vitamin C from different spirulina-based matrix formulations, with particular emphasis on the role of excipients in modulating dissolution kinetics and mechanical properties. By systematically varying the proportions of starch, microcrystalline cellulose, lactose, HPMC, and spirulina, this work aims to identify the key factors influencing vitamin C release, enhance tablet hardness, and ultimately contribute to the development of optimized nutraceutical formulations.

2. MATERIALS AND METHODS

2.1. Materials

Vitamin C (ascorbic acid) powder and its Chemical Reference Substance (CRS) were obtained from VWR (Belgium). Spirulina powder (*Arthrospira platensis*), locally sourced and characterized by fine granulometry, was used as a nutritional excipient. Pharmaceutical excipients included hydroxypropyl methylcellulose (HPMC), microcrystalline cellulose PH-102 (Avicel), maize starch, lactose (100 mesh), talc, and magnesium stearate.

2.2. Equipment

Tablet compression was performed using an alternative single-punch tablet press. Disintegration testing was carried out using a Délitest apparatus. Dissolution studies were performed using a USP type II (paddle) Dissolutest apparatus. Quantitative analysis of vitamin C was conducted using high-performance liquid chromatography (HPLC, Hitachi VWR, Belgium) equipped with a diode array detector (DAD).

2.3. Formulation of Tablets

A reference formulation previously described by Marie Miguel *et al..*, (2023) [9] was used as the baseline. Three additional formulations were prepared by varying the proportions of vitamin C and selected excipients (HPMC, starch, microcrystalline cellulose, lactose, and spirulina) (Table 1). Each batch consisted of 80 tablets, compressed under identical conditions to ensure reproducibility and comparability. The tablets obtained from each formula are presented at the figure 1.

Table 1: Composition of representative formulations (F2 vs F4)

	Formula 1	Formula 2	Formula 3	Formula 4 Reference formula
Vitamin C	32.7	32.7	6.54	6.54
Spirulina	-	-	-	26.16
HPMC	-	27.2	27.2	27.2
Starch	5.81	5.81	1.16	5.8
Avicel	14.53	14.54	2.9	14.54
Lactose	44.63	17.3	61.75	17.3
Magnesium Stearate	1.16	1.16	0.22	1.1
Talc	1.16	1.16	0.22	1.1

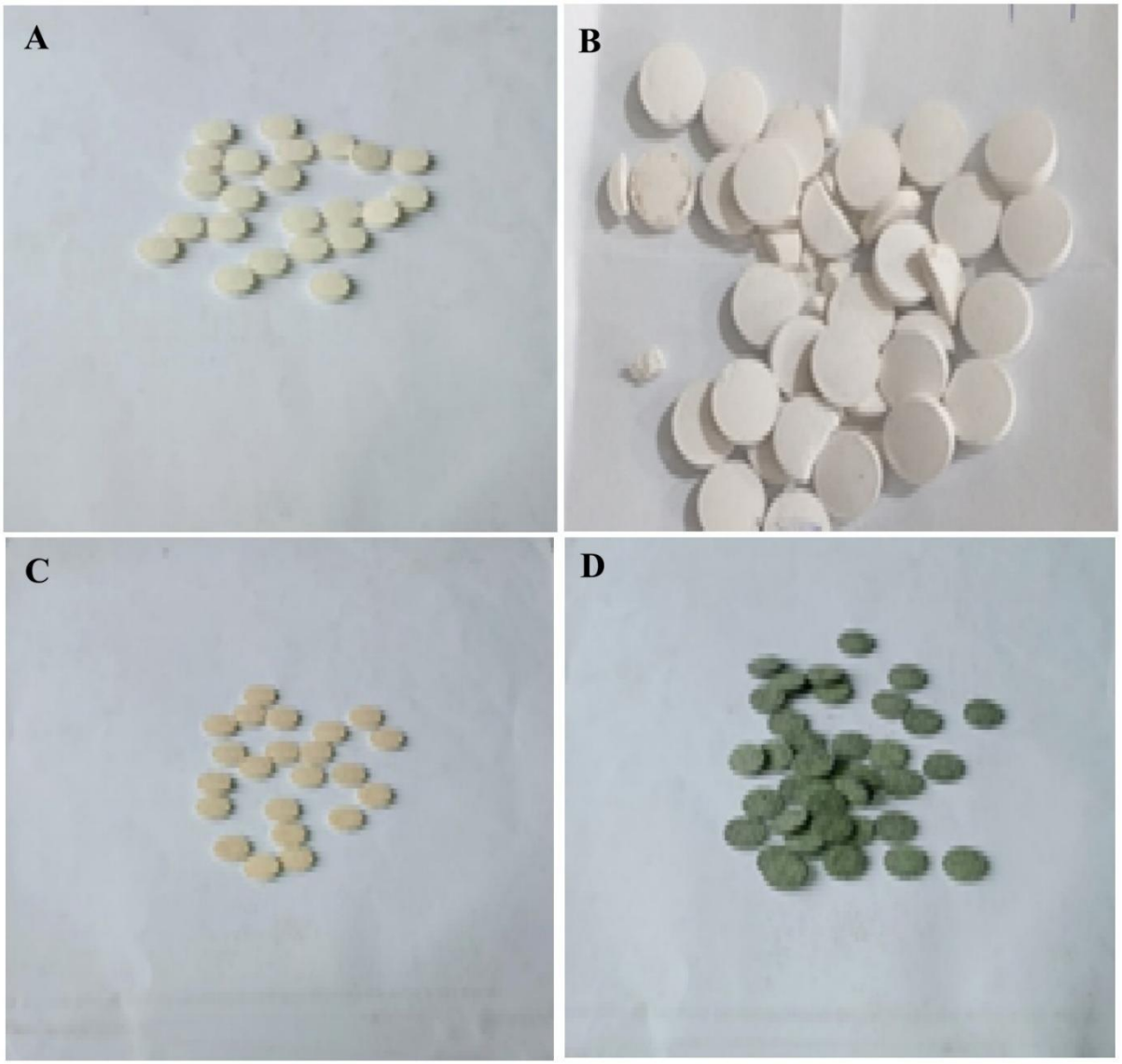

Figure 1: A (Formula 1: Round shape, Pale beige color, No break line, Tangy taste, No break line, Tangy taste.) **B** (Formula 2: Dusty appearance and cracks, round shape, light beige color without cleavage line, tangy taste.) **C** (Formula 3: Normal appearance, round shape, dark beige color without score line, tangy taste.) **D** (Formula 4: Normal appearance, round shape, pure green color without score line, slightly salty taste.)

2.4. Pharmacopeial Quality Control Tests

All tests were performed in accordance with the European Pharmacopoeia (Ph. Eur., 11th edition) and United States Pharmacopeia (USP) guidelines.

2.4.1. Mass Uniformity

Twenty tablets from each formulation were individually weighed, and the percentage deviation from the mean mass was calculated and the compliance assessed according to Ph. Eur. acceptance criteria.

2.4.2. Content Uniformity

Ten tablets per batch were powdered and analyzed by HPLC/DAD.

- **Diluent:** KH_2PO_4 buffer (2.04 g/L, pH 3) containing EDTA (0.56 g/L)
- **Mobile phase:** Methanol/phosphate buffer (5:95, v/v)
- **Column:** C18 (250 × 4 mm, 5 µm)
- **Flow rate:** 0.7 mL/min
- **Detection wavelength:** 245 nm
- **Acceptance criterion:** Acceptance Value (AV) ≤ 15

Chromatograms are provided in figures 2A, 2B and 2C.

2.4.3. Disintegration Test

Six tablets per batch were tested in distilled water at 37 ± 0.5 °C. The time required for complete disintegration was recorded.

2.4.4. Dissolution Test

Dissolution studies were conducted using the USP type II paddle method under the following conditions:

- **Medium:** 0.1 N HCl (pH 1.2), 900 mL
- **Temperature:** 37 ± 2 °C
- **Paddle speed:** 75 rpm
- **Sampling times:** 0, 15, 30, 45, 60, 120, and 240 min
- **Sample volume:** 10 mL, replaced with fresh medium to maintain sink conditions
- **Assay method:** HPLC/DAD quantification of vitamin C

2.5. Data Analysis

Dissolution profiles were compared using model-independent methods:

- **Difference factor (f_1):** values ≤ 15 indicate similarity
- **Similarity factor (f_2):** values ≥ 50 indicate similarity

Results are expressed as mean ± standard deviation (SD).

3. RESULTS

3.1. Pharmaco-technical properties

The pharmaco-technical evaluation demonstrated acceptable performance for most quality attributes across formulations. Mass uniformity complied with pharmacopeial specifications for 75% of the tested batches. Content uniformity was satisfactory for all formulations, with one batch analyzed per formulation.

In contrast, disintegration testing revealed that one formulation (F3) did not meet the acceptance criteria, indicating insufficient structural breakdown under physiological conditions.

Tablet hardness was generally improved in spirulina-containing formulations (F4) as well as in the reference formulation. This enhancement is likely attributable to the fine particle size and fibrous nature of spirulina, which promotes better interparticle bonding and compressibility during compaction [10].

3.2. Dissolution profiles

The comparative dissolution profiles of all formulations are presented in figure 2D, highlighting the sustained release behaviour of spirulina-based systems.

Significant differences were observed in the dissolution behaviour of the formulations. Comparative analysis using model-independent parameters showed that F2 and F4 were not similar, with an f1 value of 17.2. Similarly, although F3 and F4 showed an f1 value of 9.1, the corresponding f2 value of 42.75 confirmed non-similarity according to regulatory thresholds.

Overall, spirulina-containing tablets (F4) exhibited a more sustained release profile compared with the other formulations. However, a progressive decrease in measured vitamin C concentration was observed after approximately 90 minutes of dissolution testing. This behaviour is most likely related to oxidative degradation of vitamin C in the presence of spirulina-associated transition metal ions, particularly iron (Fe^{2+}), which are known to catalyze ascorbic acid oxidation reactions [11].

The role of excipients in modulating drug release was clearly demonstrated. Starch and microcrystalline cellulose (Avicel PH-102) accelerated vitamin C release, likely due to increased porosity and improved medium penetration. In contrast, HPMC acted as a hydrophilic matrix-forming polymer, resulting in a controlled and sustained release profile. Lactose exhibited a slightly inhibitory effect, potentially by modifying matrix hydration and diffusion pathways.

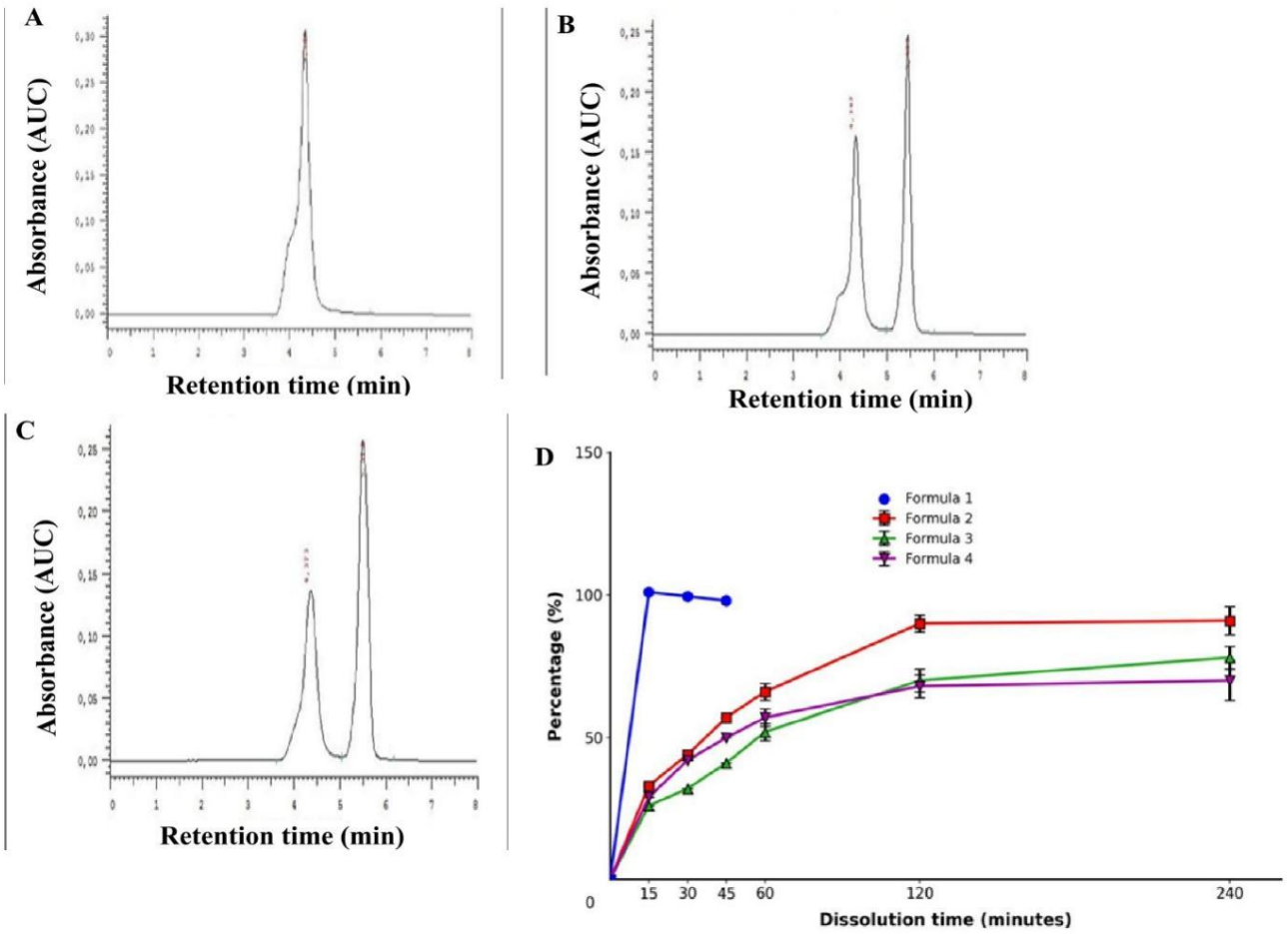

Figure 2: A (Chromatogram of Blank (KH2PO4 + EDTA mixture).) **B** (Chromatogram of the Blank and the RCS of Vitamin C.) **C** (Chromatogram of Blank and Vitamin C in a sample.) **D** (Average release profiles of vitamin C.)

4. DISCUSSION

These results show that excipient composition remains a major determinant of both the mechanical strength and the drug release behaviour of vitamin C matrix tablets [12]. The type and proportion of excipients significantly influence tablet hardness, porosity, and structural cohesion, which are critical quality attributes in solid dosage forms [13]. The inclusion of spirulina improves tablet hardness and enhances matrix integrity, contributing to better mechanical resistance during processing and storage [14]. Such reinforcement of the matrix is consistent with improvements generally observed in natural or bioactive excipient systems used in controlled release formulations [15]. However, spirulina contains pigments and bioactive compounds with potential redox activity, which may promote partial oxidative degradation of vitamin C [16]. Ascorbic acid is well known for its susceptibility to oxidation, particularly in the presence of oxygen, moisture, and reactive formulation components [17]. This degradation can reduce the effective drug content within the matrix and consequently alter the observed dissolution profile. Therefore, the release kinetics may result from a combination of diffusion-controlled mechanisms and chemical instability of vitamin C [18]. The dual effect of improved matrix densification and possible drug degradation makes the release behaviour more complex to interpret.

These findings align with recent evidence that excipients can simultaneously enhance mechanical performance while affecting drug stability in phytopharmaceutical formulations [19]. Thus, formulation optimization must carefully balance mechanical robustness with chemical compatibility to ensure performance reliability. Overall, selecting appropriate natural excipients such as spirulina requires thorough evaluation of both physicochemical stability and controlled release efficiency.

5. CONCLUSION

Spirulina-based matrix tablets demonstrated improved mechanical strength and sustained release of vitamin C. The study further confirmed that excipients significantly influence drug release behaviour: starch and microcrystalline cellulose enhanced dissolution, HPMC retarded release, and lactose slightly inhibited release.

Overall, careful optimization of excipient ratios is essential to achieve an appropriate balance between mechanical integrity and controlled release performance. Further in vivo studies are recommended to evaluate the bioavailability and therapeutic relevance of these formulations.

Conflict of interests: The authors have declared no conflicts of interest.

REFERENCES

1- Markets and Markets. Dietary supplements market: trends, opportunities, challenges [Internet]. 2024 [cited 2025 Feb 1]. Available from: https://www.marketsandmarkets.com/Market-Reports/dietary-supplements-market-782.html

2- Bendjellit M. Médicaments à base de plantes ou compléments alimentaires à base de plantes: quelles stratégies dans l'industrie pharmaceutique? [PhD thesis]. Aix-Marseille: Université d'Aix-Marseille; 2023. 131 p.

3- U.S. Food and Drug Administration (FDA). FDA 101: dietary supplements [Internet]. Silver Spring (MD): FDA; 2022 Jun 9 [cited 2025 Feb 2]. Available from: https://www.fda.gov/consumers/consumer-updates/fda-101-dietary-supplements

4- Carpenter KJ. The discovery of vitamin C. *Ann Nutr Metab*. 2012;61(3):259–64.

5- Chambial S, Dwivedi S, Shukla KK, John PJ, Sharma P. Vitamin C in disease prevention and cure: an overview. *Indian J Clin Biochem*. 2013;28(4):314–28.

6- Lykkesfeldt J, Tveden-Nyborg P. The pharmacokinetics of vitamin C. *Nutrients*. 2019;11(10):2412. doi:10.3390/nu11102412

7- Karkos PD, Leong SC, Karkos CD, Sivaji N, Assimakopoulos DA. Spirulina in clinical practice: evidence-based human applications. *Evid Based Complement Alternat Med*. 2011; 2011:531053. doi:10.1155/2011/531053

8- Novoma. Why combine spirulina and vitamin C? [Internet]. 2024 [cited 2024 Oct 16]. Available from: https://novoma.com/en/blogs/articles/spiruline-et-vitamine-c

9- Marie-Miguel G. Essai de formulation de comprimés matriciels à base de spiruline et de vitamine C [PhD thesis]. Abomey-Calavi: Université d'Abomey-Calavi; 2023. 117 p.

10- Wünsch I, Finke JH, John E, Juhnke M, Kwade A. The influence of particle size on the application of compression and compaction models for tableting. *Int J Pharm*. 2021;599:120424. doi:10.1016/j.ijpharm.2021.120424

11- Azam KR, Reza S. Formulation development using maize starch and Avicel PH101 as disintegrating agents and their effect on physical characteristics and *in vitro* release profile. *Int J Pharm Sci Res*. 2011;2(5):1070–1076.

12- Aulton ME, Taylor K. *Aulton's Pharmaceutics: The Design and Manufacture of Medicines*. 6th ed. Elsevier; 2022.

13- Rowe RC, Sheskey PJ, Quinn ME. *Handbook of Pharmaceutical Excipients*. 9th ed. Pharmaceutical Press; 2021.

14- Hamed I, Özogul F, Regenstein JM. Industrial applications of Spirulina. *Trends Food Sci Technol*. 2021;112:147–160.

15- Siepmann J, Siepmann F. Mathematical modeling of drug delivery systems. *Adv Drug Deliv Rev*. 2020;160:25–36.

16- Bechoff A, Westby A, et al. Stability of natural pigments and antioxidants in plant matrices. *Food Chem*. 2020;315:126–134.

17- Telang PS. Vitamin C in dermatology and pharmaceutical systems: stability considerations. *J Cosmet Dermatol*. 2021;20(5):1503–1512.

18- Peppas NA, Langer R. New challenges in biomaterials science. *Science*. 2022;377(6601):eabo5439.

19- Kaur G, Kaur G. Natural excipients in modern drug delivery systems. *Pharmaceutics*. 2023;15(2):512.