EJPMR, 2026, 13(8), 262-265 **Research Article** **Impact Factor: 8.158**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

DESIGN AND IN VITRO EVALUATION OF A NUTRACEUTICAL TABLET CONTAINING MIXED CAROTENOIDS FOR OCULAR HEALTH SUPPORT

Karan Singh Rathore[1]*, Prof. Dr. Pankaj Kumar Sharma[2], Prof. Dr. Jaya Sharma[3], Prof. Dr. Pankaj Sharma[4], Mr. Balbeer Singh[5]

[1]Research Scholar, Apex Institute of Pharmaceutical Sciences, Apex University, Jaipur, Rajasthan, India.
[2]Dean, Apex Institute of Pharmaceutical Sciences, Apex University, Jaipur, Rajasthan, India.
[3]Principal, Institute of Pharmaceutical Sciences, Apex University, Jaipur, Rajasthan, India.
[4]Professor, Apex Institute of Pharmaceutical Sciences, Apex University, Jaipur.
[5]Associate Professor, Apex Institute of Pharmaceutical Sciences, Apex University, Jaipur.

***Corresponding Author: Karan Singh Rathore**

Research Scholar, Apex Institute of Pharmaceutical Sciences, Apex University, Jaipur, Rajasthan, India.

DOI: https://doi.org/10.5281/zenodo.21702120

How to cite this Article: Karan Singh Rathore[1]*, Prof. Dr. Pankaj Kumar Sharma[2], Prof. Dr. Jaya Sharma[3], Prof. Dr. Pankaj Sharma[4], Mr. Balbeer Singh[5]. (2026). Design And In Vitro Evaluation Of A Nutraceutical Tablet Containing Mixed Carotenoids For Ocular Health Support. European Journal of Pharmaceutical and Medical Research, 13(8), 262–265.

Article Received on 20/06/2026 **Article Revised on 10/07/2026** **Article Published on 01/08/2026**

1. INTRODUCTION

As populations grow older, the growing prevalence causes these humanoeconomic high personal, social and economic costs diseases to develop. Eye-care capabilities may not be available especially in low middle-income countries. The macula part of the retina (the central part of your retina allowing you to read or listen), consumes more oxygen than any part of the body and is exposed to very bright light. Because of this combination, it is susceptible to damage from reactive oxygen species generated during normal visual activity. Through the years, oxidative stress causes the degeneration of photoreceptors and retinal pigment epithelium (RPE), resulting in AMD. Carotenoids cannot be formulated into a tablet because of its physicochemical properties. All three of the active ingredients are classified as BCS Class II which means that they will easily cross biological membranes but poorly soluble in the water. The extended conjugated double-bond system is highly sensitive to light, heat, and oxygen and thus destructs before it reaches the patient. To ensure stability, it is necessary to carefully select excipients and processing conditions. Pro-vitamin A tablet was produced through a technique called direct compression. The direct compression was preferred over wet granulation due to moisture and heat action of wet granulation, which is harmful to carotenoids. Both factors amplify the degradation of carotenoids.

2. Drug Profile

This study used three actives, all chosen for their known importance to ocular antioxidant defence.

2.1 Lutein

Lutein ($C_{40}H_{56}O_2$, MW 568.87 g/mol); It is a xanthophyll carotenoid obtained mainly from marigold (Tagetes erecta) petals. It is a dark orange crystalline powder, practically insoluble in water, and highly lipophilic (log P ~7.0). It is the major pigment of the macular periphery, where it filters blue light and quenches singlet oxygen. The AREDS2 dose of 10 mg/day was used in this formulation.

2.2 Zeaxanthin

Zeaxanthin ($C_{40}H_{56}O_2$, MW 568.87 g/mol) is a structural isomer of lutein obtained from pepper or wolfberry extracts. It exhibits a preferential concentration at the fovea's centre, where light intensity is greatest; it is one of the most effective natural singlet oxygen quenchers. The dose of 2 mg/day used was AREDS2.

2.3 Astaxanthin

Astaxanthin, a ketocarotenoid ($C_{40}H_{52}O_4$; MW 596.84 g/mol) from Haematococcus pluvialis microalga. The keto and hydroxyl groups in it endow it with an unusual strong and broad antioxidant capacity for protection of both cell surface and interior of membranes. It can also cross the blood-retinal barrier and access retinal tissue

directly. Usage was within permissible limits as per FSSAI; 4 mg/day. The three carotenoids are nearly insoluble in water but quite lipophilic (log P values of about 6 and nearly 15). Thus, their absorption in the body depends largely on their being dissolved in bile-salt micelles and dietary fat.

2.4 Key Excipients

Microcrystalline cellulose (MCC PH-102), and spray-dried lactose were used as diluents to impart the adequate flow and compressibility to the powder blend. Colloidal silicon dioxide was used as glidant. Crospovidone was used as a superdisintegrant. PVP K-30 was used as a dry binder. Magnesium stearate was used as lubricant. Vitamin C was included as a sacrificial antioxidant to protect the carotenoids from oxidation while polysorbate 80 was included as a wetting agent to aid dissolution of these highly lipophilic actives.

3. AIM AND OBJECTIVES

Aim: To design, develop, and evaluate an oral nutraceutical tablet combining lutein, zeaxanthin, and astaxanthin in evidence-based doses, using direct compression technology, as a stable and effective supplement for supporting ocular health.

OBJECTIVES

- To review the pharmacological and formulation literature relevant to ocular carotenoid nutraceuticals.
- To develop six tablet formulations (F1–F6) by direct compression, varying disintegrant and antioxidant levels.
- To evaluate pre-compression powder flow properties (bulk/tapped density, Carr's Index, Hausner Ratio, angle of repose).
- To perform post-compression quality control tests: weight variation, hardness, friability, thickness, disintegration time, and content uniformity.
- To study in vitro drug release and fit the data to standard release-kinetic models.
- To assess antioxidant activity of the optimised formulation using the DPPH assay.
- To carry out short-term accelerated stability testing (40°C/75% RH, 90 days) on the optimised formulation.
- To identify, using statistical analysis, the best-performing formulation among F1–F6.

4. MATERIALS AND METHODS

Certified pharmaceutical-grade suppliers provided lutein, zeaxanthin, and astaxanthin. The excipients which were used were MCC PH-102, spray-dried lactose, crospovidone, PVP K-30, magnesium stearate, colloidal silicon dioxide, ascorbic acid and polysorbate 80, which were nf/usp/ep grade.

Development of six formulations (F1-F6) was based on constant active dose of 10 mg lutein, 2 mg showing and 4 mg astaxanthin keeping the MCC:lactose diluent ratio, crospovidone concentration (2-6%) and ascorbic acid (1-2%) varying. The ingredients were sifted, blended and diluted geometrically using double-cone blender. We used a 10-station rotary tablet press with flat faced punches (9 mm) which compressed the mixture for 5–8 kg/cm² hardness.

Analysis of bulk density, tapped density, Carr's index, Hausner ratio and angle of repose was performed on the blends obtained by pre-compression. Compatibility of the drug and excipients was checked by FTIR and DSC method.

Once the tablets underwent compression, they were subjected to a series of evaluations, including weight comparison, hardness test, friability test using Roche friabilator (applying 100 rotations), and thickness evaluation, disintegration time (in phosphate buffer at pH 6.8, 37°C) was also evaluated. Further we conducted a drug content uniformity test with the help of UV spectroscopy (at 446 nm).

The dissolution of the formulation was determined in vitro using USP Type II (paddle) apparatus at a constant stirring speed of 50 rpm, in phosphate buffer pH 6.8 containing polysorbate 80 (0.5%). Sample was withdrawn over a period of 60 minutes. Examination of the zero-order first-order Higuchi Korsmeyer-Peppas Hixson-Crowell kinetic models.

The most effective formulation underwent testing for its antioxidant activity by utilizing DPPH radical scavenging assay for the IC_{50} value calculations with ascorbic acid as the reference standard. The optimized batch was conditioned for 90 days at 40 ± 2°C / 75 ± 5% RH as per ICH Q1A (R2) to assess its appearance, hardness, drug content, dissolution and DPPH activity on 0, 30, 60 and 90 days. We conducted a One Way ANOVA along with Tukey's post hoc test to show statistical significant in dissolution performance among formulations ($p < 0.05$).

5. RESULTS AND DISCUSSION

All six powder blends showed good flow properties, with Carr's Index between 14.5% and 15.8%, Hausner Ratio between 1.16 and 1.19, and angle of repose between 26.5° and 28.4° — all within the acceptable range for direct compression. FTIR and DSC studies showed no shift or loss of the characteristic carotenoid peaks in the physical mixtures, confirming that the actives and excipients were chemically compatible.

All six formulations met pharmacopoeial limits for weight variation, hardness (5.4–6.2 kg/cm²), friability (well under 1.0%), and drug content (97.4–99.3% of label claim). Disintegration time decreased as crospovidone concentration increased, with F4 giving the fastest disintegration (8.4 minutes).

Formulation F4 (20 mg crospovidone, 10 mg ascorbic acid, MCC:lactose 100:95) gave the best overall performance, with the shortest disintegration time, highest drug release (89.7% at 60 minutes), and best content uniformity. Dissolution followed the Higuchi model most closely (R^2 = 0.9912), with Korsmeyer–Peppas exponents of 0.41–0.44 indicating Fickian (diffusion-controlled) release. One-way ANOVA confirmed a statistically significant difference in dissolution among formulations ($F = 15.42$, $p < 0.0001$), and Tukey's test showed F4 was significantly better than F1, F2, and F3, while being statistically comparable to F5 and F6 — F4 was selected based on its overall superior physical quality and antioxidant performance.

Over 90 days of accelerated storage (40°C/75% RH), F4 remained within specification: hardness and friability changed only marginally, drug content stayed above 96%, dissolution remained above 87%, and DPPH IC_{50} stayed below 14 µg/mL. A slight fading of colour was observed but was considered a minor cosmetic change rather than a sign of significant degradation.

Table 1: Post-Compression Quality Summary (Selected Formulations).

Parameter	F1	F4 (Optimised)	F6
Hardness (kg/cm²)	5.4	6.2	5.9
Friability (%)	0.68	0.52	0.58
Disintegration time (min)	12.6	8.4	9.1
Drug content (%)	97.4	99.3	97.9
Dissolution at 60 min (%)	78.4	89.7	86.1

Table 2: Stability of Optimised Formulation (F4) at 40°C/75% RH.

Parameter	Day 0	Day 30	Day 60	Day 90
Hardness (kg/cm²)	6.2	6.1	6.0	5.9
Drug content (%)	99.3	98.6	97.8	96.4
Dissolution at 60 min (%)	89.7	89.2	88.6	87.8
DPPH IC_{50} (µg/mL)	12.34	12.68	13.12	13.74

Taken together, these results indicate that the carotenoid combination is chemically well protected within this tablet matrix, most likely due to the combined effect of the ascorbic acid sacrificial antioxidant, the low-moisture excipient system, and the desiccant-protected packaging used during storage. The overall pattern of gradual, low-magnitude change across all tested parameters is consistent with a formulation that would be expected to meet a standard shelf-life specification under normal storage conditions, though real-time (long-term) stability data would be needed to confirm an actual shelf life.

6. CONCLUSION

A nutraceutical tablet made from a stable direct compression containing lutein (10 mg), zeaxanthin (2 mg) and astaxanthin (4 mg) was successfully developed and evaluated. The compatibility of actives and excipients was assured following preformulation studies and all six trial formulations conformed to standard pharmacopoeial quality. The formulation F4 was noted to be optimum because it had the fastest disintegration, highest drug release, best content uniformity, and strongest antioxidant activity. Additionally, the formulation was physically and chemically stable for 90 days of accelerated storage. These in vitro findings support the scientific and technical feasibility of a mixed-carotenoid tablet as a practical evidence-based nutraceutical for ocular health support, and provide a basis for future in vivo and clinical evaluation.

7. REFERENCES

1. Halliwell B, Gutteridge JMC. Free Radicals in Biology and Medicine. 5th ed. Oxford: Oxford University Press, 2015.
2. Hahn P, Milam AH, Dunaief JL. Maculas affected by age-related macular degeneration contain increased chelatable iron in the retinal pigment epithelium and Bruch's membrane. Arch Ophthalmol., 2003; 121(8): 1099-1105.
3. Porter NA, Caldwell SE, Mills KA. Mechanisms of free radical oxidation of unsaturated lipids. Lipids, 1995; 30(4): 277-290.
4. Uchida K. Role of reactive aldehyde in cardiovascular diseases. Free Radic Biol Med., 2000; 28(12): 1685-1696.
5. Delori FC, Dorey CK, Staurenghi G, Arend O, Goger DG, Weiter JJ. In vivo fluorescence of the ocular fundus exhibits retinal pigment epithelium lipofuscin characteristics. Invest Ophthalmol Vis Sci., 1995; 36(3): 718-729.
6. Friguet B, Stadtman ER, Szweda LI. Modification of glucose-6-phosphate dehydrogenase by 4-hydroxy-2-nonenal. Formation of cross-linked protein that inhibits the multicatalytic protease. J Biol Chem., 1994; 269(34): 21639-21643.
7. Spector A. Oxidative stress-induced cataract: mechanism of action. FASEB J., 1995; 9(12): 1173-1182.
8. Solvent-Free Oil-Based Extraction and Microencapsulation of Lutein from Marigold (*Calendula officinalis*). *Molecules*, 2026; 31(10): 1649.

9. Exploring Cyclodextrin Complexes of Lipophilic Antioxidants: Benefits and Challenges in Nutraceutical Development. *International Journal of Molecular Sciences*, 2025; 26(23): 11682.
10. S. J. Kshirsagar, Abhish Jadhav, Saad Ansari*, Formulation, Development, and Evaluation of Polyherbal Geltab System for Manifestation of Hemorrhoids, Int. J. of Pharm. Sci., 2025; 8: 1503-1507.
11. Arshad MT, Maqsood S, Ikram A, Khan AA, Raza A, Ahmad A, Gnedeka KT. Encapsulation Techniques of Carotenoids and Their Multifunctional Applications in Food and Health: An Overview. Food Sci Nutr., 2025 May 20; 13(5): e70310.
12. Zhang, J., Wu, M., Chen, Y., et al. Beneficial effects of astaxanthin in ocular diseases: a comprehensive review. *Frontiers in Medicine (Lausanne)*, 2023; 10: 1145107.
13. Ma Y, Li C, Xiu W, Wang X. In vivo and in vitro evaluation of stability and antioxidant activity of lycopene-nanostructured lipid carriers. Food Sci Biotechnol., 2022 Dec 13; 32(6): 833-845.
14. Microemulsion-based lutein extraction from marigold petals: Process optimization and stabilization evaluation. *Food and Bioproducts Processing (ScienceDirect)*, 2023.
15. Liu, W.-Y., Hsieh, Y.-S., Ko, H.-H., & Wu, Y.-T. Formulation Approaches to Crystalline Status Modification for Carotenoids: Impacts on Dissolution, Stability, Bioavailability, and Bioactivities. *MDPI*, 2023.
16. Liu, Q., Lin, Y., Li, J., Wang, Y., Li, S., Bian, H., Zhang, W., & Wu, Z. (2023). Microemulsion-basedch lutein extraction from marigold petals: Process optimization and stabilization evaluation. Industrial Crops and Products, 195: 116454.