Effect of Co-Encapsulated Natural Antioxidants with Modified Starch on the Oxidative Stability of β-Carotene Loaded within Nanoemulsions

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Abstract: β-Carotene (vitamin A precursor) and α-tocopherol, the utmost energetic form of vitamin E (VE), are known to be fat-soluble vitamins (FSVs) and essential nutrients needed to enhance the growth and metabolic functions of the human body. Their deficiencies are linked to numerous chronic disorders. Loading of FSVs within nanoemulsions could increase their oxidative stability and solubility. In this research, VE and β-Carotene (BC) were successfully co-entrapped within oil-in-water nanoemulsions of carrier oils, including tuna fish oil (TFO) and medium-chain triglycerides (MCTs), stabilized by modified starch and Tween-80. These nanoemulsions and free carrier oils loaded with vitamins were stored for over one month to investigate the impact of storage circumstances on their physicochemical characteristics. Entrapped bioactive compounds inside the nanoemulsions and bare oil systems showed a diverse behavior in terms of oxidation. A more deficiency of FSVs was found at higher temperatures that were more noticeable in the case of BC. VE behaved like an antioxidant to protect BC in MCT-based nanoemulsions, whereas it could not protect BC perfectly inside the TFO-loaded nanoemulsions. However, cinnamaldehyde (CIN) loading significantly enhanced the oxidative stability and FSVs retention in each nanoemulsion. Purity gum ultra (PGU)-based nanoemulsions comprising FSVs and CIN presented a greater BC retention (42.3%) and VE retention (90.1%) over one-month storage at 40 °C than Tween 80. The superior stability of PGU is accredited to the OSA-MS capabilities to produce denser interfacial coatings that can protect the entrapped compounds from the aqueous phase. This study delivers valuable evidence about the simultaneous loading of lipophilic bioactive compounds to enrich functional foods.

Keywords: fat-soluble vitamins; cinnamaldehyde; nanoemulsions; purity gum ultra; physicochemical stability
1. Introduction

Fat-soluble vitamins (FSVs) are biologically active compounds with numerous therapeutic biological roles and are known to be essential nutrients that can enhance the growth and metabolic functions of the human body. Among FSVs, α-tocopherol (the utmost energetic form of vitamin E) and β-carotene (vitamin A precursor) have been exploited as potent antioxidant agents. In previous studies, it has been well clarified that chronic ailments, including aging, cancers, diabetes, and cardiovascular disorders, can be reduced by the consumption of FSVs [1–3]. Thus, the food industries are showing their keen attention in the production and enrichment of diverse functional foods such as supplements and beverages with lipophilic b, e.g., ω-3 fatty acids, curcuminoids, and FSVs [4,5]. Though, the addition of lipophilic bioactives into the aqueous-based food matrices is restricted because of their structure break-down and poor solubility nature, as well as high sensitivity to environmental temperature, oxygen, and light [6].

Various lipid-based and biopolymeric nanocarriers have been established, including nanoemulsions, nanoliposomes, nanohydrogels, and solid-lipid nanoparticles for the entrapment of vitamins [6–8]. Among these, oil-in-water (O/W) nanoemulsions have been considered to be efficient delivery systems because of their superior stability in contradiction of gravitational separation, flocculation, and coalescence [9]. However, the nanometric diameter of nanoemulsions provides a higher surface area that facilitates interaction between the aqueous phase and unsaturated lipids present in the dispersed phase droplets, which are known to be extremely susceptible to oxidation [10,11]. On the other hand, the structural composition of nanoemulsions, particularly the type of antioxidants, carrier oils, OSA-modified starch, can leave negative impacts on the oxidation of loaded lipophilic bioactive compounds [12,13].

It should be noted that FSVs first need to be dissolved into an appropriate carrier oil before loading into the nanoemulsions. Previous literature has revealed that since carrier oils have a higher unsaturation degree, they exhibit poor stability in the direction of oxidation rather than those oils that have lower unsaturation levels [14,15]. For this purpose, antioxidants have been recognized as promising candidates, which are being used to avoid oxidation issues of lipid-based matrices; though, the behavior of each antioxidant agent could be different for each system; because oxidation is a complicated phenomenon [16,17]. For instance, Chaiyasit et al. [18] reported that α-tocopherol was more effective as compared to δ-tocopherol inside the menhaden oil; but they found a different trend in terms of antioxidant effect inside the menhaden oil-loaded emulsions. In addition, butylated hydroxyl toluene (BHT) displayed an identical efficiency in each formulation of emulsions. In another research, Serfert et al. [19] found dissimilar properties of lecithin when combined with ascorbyl palmitate used for O/W nanoemulsions rather than spray-dried nanoemulsions.

Usage of innovative techniques has become common for production and processing [20–23]. Recently, there is a growing interest in the use of natural antioxidants instead of synthetic ones due to consumer preference for natural ingredients [24–26]. Cinnamon is recommended as an ancient spice that encompasses cinnamaldehyde, has been exploited as an antioxidant, anticancer, anti-inflammatory, antimicrobial, and insecticidal agent [27,28]. Additionally, it has been gained safe status by the Joint WHO/FAO Expert Committee on Food Additives [29]; thus, being used as an antioxidant in the nano-emulsified systems [30].

Emulsifiers can decrease the interfacial tension among the aqueous and lipid phase as well as their outstanding characteristics, such as layer thickness, binding capacity, and surface charge, which could contribute to improving the bioactivity and stability of entrapped bioactive compounds [31–33]. Among biopolymer-based emulsifiers, modified starches have been successfully used owing to their superior stability against ionic strength, a diverse range of pH values, and higher temperatures. Octenyl succinic anhydride-modified starches (OSA-MS) have also been used in several investigations as emulsifiers and stabilizers for entrapment of various lipophilic bioactive compounds, such as FSVs, curcumin, flavoring oils, and resveratrol [9,34,35].
Herein, the aim of this study was to fabricate FSVs-loaded nanoemulsions stabilized by OSA-MS and Tween 80. In addition, the effect of co-entrapped antioxidants (cinnamaldehyde) and carrier oils was also investigated.

2. Materials and Methods

2.1. Materials

Tuna fish oil as a long-chain triacylglycerol was kindly gifted by Novosana (Taicanag) Ltd., (Suzhou, China). Medium-chain triacylglycerols (MCTs) with capric acid (∼44%) and caprylic acid (∼56%) were supplied by TA Foods Ltd. (Yorkton, SK, Canada) and Stepan (Maywood, NJ, USA). OSA-modified starch (Purity Gum Ultra, PGU) was bought from Ingredion China Limited (Shanghai, China). Tween-80 (TW-80) was provided by Sinopharm Chemical Reagents Co., Ltd. (Shanghai, China). β-Carotene (BC) and α-tocopherol (VE) with ≥97.0% purity were obtained from Sigma-Aldrich (St. Louis, MO, USA). Cinnamaldehyde (CIN) (>98%) was purchased from Jian Ju Peng Natural Flavor Oil Co LTD (Jilin, China). Double distilled water was used for all aqueous solutions, and all other reagents and chemicals used in this study were of analytical grade.

2.2. Preparation of Nanoemulsion

The aqueous suspension was prepared by dissolving modified starch (PGU, 1.5% w/w) into double distilled water and kept stirring for the whole night at 30 °C in order to confirm perfect hydration. Aqueous suspension of Tween-80 (TW) was also dispersed (2% w/w) into double distilled water while stirring for 1 h at 25 °C. In the next stage, diverse concentrations of different bioactives (0.1% (w/w) of BC, 2% and 3% (w/w) of VE, and 1% (w/w) of CIN) were loaded into TFO and MCT oils for fabrication of lipid phases (10% w/w) as illustrated in Figure 1. In brief, 0.1% (w/w) of BC was dispersed into oil TFO and MCT and stirred for 10 min at 55 °C, followed by further stirring for 1 h at 25 °C in order to confirm perfect dissolvation. After 45 min, 2% and 3% (w/w) of VE was poured into the BC-loaded oil phase with additional stirring for 60 min. Next, 1% (w/w) of CIN was added inside the vitamin-loaded oil phase while stirring over 10 min. Then, nanoemulsions were formulated by adopting the way proposed formerly by Rehman et al. [9], with minor amendments. Firstly, the oil phase was added into aqueous at a ratio of 10:90 and then homogenized by Ultra-Turrax for 3–4 min at 18,000 rpm to obtain coarse emulsions. Secondly, 40 mL of coarse emulsions were proceeded to ultrasonication (40% of the maximum power at 13 min) to achieve nanoemulsions. In this regard, an ultrasonic processor (JY98-IIIDN, Ningbo Scientz Biotechnology Co., Ningbo, China) with a 20 mm probe diameter, with a maximum power of 1200 W and a frequency of 20 kHz, was applied. Sonication processing time and resting time were put at 5 and 7 s, respectively. Throughout the ultrasonication process, the temperature of all nanoemulsions was maintained through ice jackets and observed by a thermometer.

2.3. Measurement of Mean Particle Size (MPS), Zeta-Potential (ZP), and Polydispersity Index (PDI)

MPS, PDI, and ZP of nanoemulsions were examined through Zetasizer (Nano-ZS90, Malvern Instruments, Malvern, UK) according to the dynamic light scattering (DLS) technique at room temperature by adopting the procedure of Rehman et al. [9]. All formulations were diluted 200 times with distilled water to minimize scattering prior to the measurements and stirred to make sure consistency among samples. Every analysis was carried out three times. The surface charge on all nanoemulsion particles was obtained by 100-times dilution.
2.4. Storage Stability of Vitamin-Loaded Nanoemulsions

All nanoemulsions were packed into tightly capped glass bottles directly after fabrication and kept at 25 and 40 °C for 30 days in the shady apartment. Each collected nanoemulsions was analyzed occasionally in terms of MPS, oxidative stability, and entrapped contents of vitamins (VE and BC).

2.4.1. Measurement of Peroxide Value (POV)

Lipid hydroperoxides of freshly prepared nanoemulsions and one-month stored nanoemulsions at 25 °C were analyzed based on oxidative stability according to the procedure proposed by Rashidinejad et al. [36], with minor modifications. Briefly, about 1 mL of each nanoemulsion sample was combined with isooctane: 2-propanol (2:1 \(v/v\)) and vortexed 3-times (10 s each time). Next, centrifuged at 1300 \(\times\) g for 3 min, and the solvent phase was collected, which was then added to 3.2 mL of 2:1 \(v/v\) methanol/1-butanol mixture with the addition of 3.94 M ferrous iron reagent/ammonium thiocyanate (1:1 \(v/v\); 30 mL). After 20 min in the dark, it was analyzed at 510 nm wavelength in a UV-visible spectrophotometer (Beckman Coulter Inc., Fullerton, CA, USA). Each sample was analyzed in triplicate.

2.4.2. Measurement of Thiobarbituric Acid Reactive Substances (TBARS)

TBARS, secondary oxidative products were analyzed by following the procedure of Qiu et al. [37], with small variations. First, a solution of thiobarbituric acid (TBA) was made by mixing 0.375 g of TBA, 15 g of trichloroacetic acid, 1.76 mL of 12 M HCl, and 82.9 mL of deionized water. For the analysis, 0.5 mL sample of oil or nanoemulsion was mixed with 2.5 mL of TBA solution in test tubes and heated for 15 min in a hot water bath at 25 °C. After this step, tubes were cooled down with tap water for 10 min and then centrifuged at 11,000 \(\times\) g for 15 min. The absorbance of all samples was observed at 532 nm using a UV-VIS spectrophotometer (Synergy HT, BioTek Instruments Inc., Winooski, VT, USA). The TBARS concentration was accessed by means of a 1,1,3,3-tetraethoxypropane
standard curve (standard curve equation $Y = 0.7499X + 0.0366$ and coefficient correlation ($R^2$) = 0.9968). Each sample was analyzed in triplicate.

2.4.3. Measurement of BC by HPLC

To extract BC contents, 0.4 mL of each emulsion was packed in a glass tube. In brief, 1 mL of dimethyl sulfoxide was added to the emulsion sample inside the glass tube and vortexed for 3 min in order to de-emulsify the nanoemulsion. For extraction of BC contents, a 4 mL combination of dichloromethane/n-hexane (1:4 v/v) was poured into the de-emulsified sample. The obtained extracts were poured using a nylon syringe (having filter diameter of 0.22 µm) into a 2 mL amber container. After that, BC contents were measured using HPLC by adopting the procedure proposed by Yi et al. [38] in triplicate. The standard curve among BC contents and absorption peak area was designed and fitted using a linear function. All values were presented as the BC retentions, which are well-defined employing $C_t / C_o$, where $C_t$ is the BC contents at storage time, and $C_o$ is the preliminary BC contents accessed directly after fabrication of all nanoemulsions.

2.4.4. Measurement of VE by HPLC

To extract VE contents, 0.05 mL of the emulsion was de-emulsified by using 0.2 mL of dimethyl sulfoxide followed by incorporation of 5 mL composition of acetonitrile/methanol (3:97 v/v). Briefly, a 0.22 µm nylon syringe filter was used to suck the aforementioned extract, which was shifted into a 1.5 mL amber container. Next, HPLC was used to measure the VE concentration by adopting the method of Hategekimana et al. [39], with slight amendments in triplicate. The standard curve among VE contents and absorption peak area was designed and fitted using a linear function. All results were stated as the VE retentions, which are well-defined by means of $C_t / C_o$, where $C_t$ is the VE contents at storage time, and $C_o$ is the primary VE contents accessed directly after construction of all nanoemulsions.

2.5. Statistical Analysis

The experimental data were evaluated using Minitab 17 (Minitab Inc., State College, PA, USA) and one-way ANOVA; the significant differences among samples were analyzed with Duncan’s multiple range test on a 95% confidence level ($p \leq 0.05$).

3. Results and Discussion

3.1. Physicochemical Stability of Vitamin-Loaded Nanoemulsions

3.1.1. MPS, ZP, and PDI of BC- and VE-Loaded Nanoemulsions

In this study, three bioactive compounds, i.e., BC, CIN, and VE, were loaded within the emulsion-based matrices by using two kinds of carrier oils, which were emulsified by PGU and TW-80. In the primary section, BC alone and with diverse levels of VE were loaded into TFO and MCT-based lipid phases, stabilized by PGU. Nanoemulsions comprising 0.1% w/w BC-loaded TSO (NE1) and MCT (NE2) exhibited a droplet size < 250 nm, as illustrated in Table 1. On the other side, mixtures of BC with diverse levels (2% and 3% w/w) of VE were equipped in both kinds of carrier oils, which were loaded into nanoemulsions emulsified by PGU and TW-80. An increment in MPS was observed for NE3 and NE5, both encompassing 2% VE, and nanoemulsions (NE4 and NE5) enriched with 4% VE showed NPS above 250 nm [40].

It has been concluded in previous studies that, incorporation of the maximum quantity of VE in any nano-emulsified system reduces the droplet size owing to the interfacial tension lowering effect of CIN [39,41]. PDI, a significant factor, has known to evaluate the distribution of particle size of any nano-emulsified system; thereby, smaller PDI results elaborate fine and smooth distribution of fabricated particles [9]. Table 1 clearly depicts that VE loading could not exhibit any significant influence on PDI as well as there was no direct relationship observed among the kinds of carrier oils and PDI variations. ZP is a key parameter that is used for evaluating the stability of emulsion-based matrices; thus, greater ZP values (>±30) are well thought-out to offer superior stability to the emulsified systems [42]. Nanoemulsions coded by NE1, NE3, and NE5 holding TFO displayed greater
ZP rather than MCT-loaded nanoemulsions (NE2, NE4, and NE6). In addition, the VE loading resulted in a decrease in the ZP values except for NE4. A negative charge on the exterior layers of OSA-MS is accredited to the succinylation used for modification of native starches. A very minor disparity in ZP findings of all nanoemulsions might be owing to the existence of diverse nature of oil combinations as well as entrapped lipophilic bioactive compounds [43].

Table 1. Effect of carrier oils, emulsifiers, and entrapped bioactive compounds on MPS, ZP, and PDI of produced nanoemulsions.

| Nanoemulsions Sample Codes | Emulsifier Type | Oil Type | Bioactive Type | MPS (nm) | ZP (mV) | PDI |
|---------------------------|----------------|----------|----------------|---------|---------|-----|
| NE1                       | PGU            | TFO      | BC (0.2%)      | 235 ± 2.23 c | −38.2 ± 1.34 | 0.162 ± 0.023 |
| NE2                       | PGU            | MCT      | BC (0.2%)      | 233 ± 1.42 c | −33.6 ± 0.45 | 0.134 ± 0.009 |
| NE3                       | PGU            | TFO      | BC (0.2%) + VE (2%) | 246 ± 3.12 b | −38.4 ± 0.76 | 0.129 ± 0.049 |
| NE4                       | PGU            | MCT      | BC (0.2%) + VE (2%) | 243 ± 1.45 b | −35.6 ± 0.54 | 0.112 ± 0.045 |
| NE5                       | PGU            | TFO      | BC (0.2%) + VE (3%) | 257 ± 4.67 a | −33.9 ± 0.32 | 0.147 ± 0.078 |
| NE6                       | PGU            | MCT      | BC (0.2%) + VE (3%) | 252 ± 3.22 a | −33.1 ± 0.92 | 0.103 ± 0.035 |
| NE7                       | PGU            | TFO      | BC (0.2%) + CIN (1%) | 222 ± 4.34 b | −35.1 ± 0.07 | 0.132 ± 0.003 |
| NE8                       | PGU            | MCT      | BC (0.2%) + CIN (1%) | 224 ± 5.87 a | −33.7 ± 0.65 | 0.092 ± 0.075 |
| NE9                       | PGU            | TFO      | BC (0.2%) + VE (2%) + CIN (1%) | 244 ± 3.12 b | −31.3 ± 0.34 | 0.083 ± 0.062 |
| NE10                      | PGU            | MCT      | BC (0.2%) + VE (2%) + CIN (1%) | 232 ± 4.89 b | −29.7 ± 0.89 | 0.010 ± 0.013 |
| NE11                      | TW-80          | TFO      | BC (0.2%) + VE (2%) + CIN (1%) | 186 ± 3.41 c | N/D | N/D |
| NE12                      | TW-80          | MCT      | BC (0.2%) + VE (2%) + CIN (1%) | 181 ± 3.18 c | N/D | N/D |

Values with different letters are significantly different (p < 0.05).

3.1.2. Impact of Storage Conditions on Vitamin-Loaded Nanoemulsions

Storage time and temperature are those parameters that can be used to assess the stability of nanoemulsions. In order to observe the coalescence, Ostwald ripening and flocculation phenomena, all formulations were stored for 30 days at 25 and 40 °C, as well as to access the effect of storage time and temperature on mean droplet size with the aim of determining the stability of all emulsions. In order to explore the influence of temperature and time on MPS, nanoemulsions having codes (NE1-NE6) comprising BC alone or combined with VE were stored at 25 and 40 °C over 30 days. After storage of 30 days, all nanoemulsions that were kept at 25 °C showed more stability, and an extreme increment in MPS around 21 nm was observed in the case of NE6 nanoemulsion, as portrayed in Figure 2A. NE3 nanoemulsion presented the smallest increase in MPS, about 9 nm over 30 days’ storage. At 40 °C, all nanoemulsions displayed a significant increase in MPS and MCT-loaded nanoemulsions encapsulating BC and VE represented as NE4 and NE6 showed an extreme rise in MPS (∼29 nm), as expressed in Figure 2B. Many researchers have covered the increasing phenomenon of MPS caused by storage circumstances in their investigations [9,44,45]. As an example, Zhao and co-workers found superior stability of nanoemulsions enriched with FSO as compared to MCT because of greater interfacial tension among aqueous suspension of nanoemulsion and FSO [45].

3.1.3. Oxidative Stability of Vitamin-Loaded Nanoemulsions

Nanoemulsions having codes (NE1-NE6) were kept at 25 °C in order to access the primary and secondary oxidation stability. Figure 3A,B shows that TFO-loaded nanoemulsions produced greater POV and TBARS oxidative products rather than MCT entrapped nanoemulsions. Additionally, NE5 nanoemulsions equipped by TFO, BC, 3% w/w VE had presented more instability in terms of oxidation. The MCT-loaded nanoemulsions showed higher stability toward oxidation that might be owing to containing medium-chain triglycerides, which are known for being less vulnerable toward oxidation rather than long-chain triglycerides [46]. In our earlier research, the oxidative instability of borage seed oil-loaded nanoemulsions was observed significantly [9]. In this study, loading of
BC and VE could not deliver safety; therefore, nanoemulsions encompassing 3% w/w VE presented higher oxidative instability. For instance, Sánchez et al. [47] observed more oxidative instability in emulsified systems encapsulating polyunsaturated oil and VE during storage. This contradicts with renowned phenomenon “polar paradox” that elaborated that hydrophobic and hydrophilic natural antioxidants could perform suitable results inside the emulsion-based matrices as well as in free oils, respectively. Though, numerous researches have successfully proved wrong to this hypothesis [48,49]. In order to investigate the oxidative behavior (primary and secondary oxidative products), free carrier oils, i.e., TFO, MCT, or both enriched with BC and 2% w/w VE, were kept at 25 °C. For this purpose, Figure 3C clearly depicts that both oils (TFO and MCT) showed diverse attitudes for POV. TFO alone or in combination with any studied bioactive compounds was found to be more unstable owing to more production of POV, but MCT alone or in combination with any studied bioactive compounds revealed more stability toward oxidation. In the case of secondary oxidation, TFO combined with 2% (w/w) VE had presented higher TBARS values, as illustrated in Figure 3D. MCT alone or in combination with any studied bioactive compounds proposed a minor rise in TBARS as compared to POV findings but results were significantly less rather than TFO. Our results about primary and secondary oxidative products were in accordance with findings of Jacobsen and his group [50]. Again, the greater stability of bare MCT alone in combination with bioactive compounds in terms of oxidation might be due to medium-chain triglycerides including capric acid and caprylic acid. The oxidation values of TFO seem very interesting and unique. The loading of 2% w/w VE resulted in a significant rise in the case of POV; on the other side, there was no significant influence observed on TBARS results for TFO alone after storage of 30 days, as explained in Figure 3C,D. Nevertheless, due to the loading of BC, a reduction in oxidation phenomenon was reported instead of TFO alone. In conclusion, the oxidation findings of the current study exposed that loading of VE in highly unsaturated free oil did not perform well being an antioxidant owing to the production of hydroperoxides through the accretion of tocopherols radicals. Our results were supported by the theory of the “polar paradox” and found to be in accordance with the discoveries of Chaiyasit et al. [18] and Serfert et al. [19]. The amount of an antioxidant could play a crucial part in governing oxidation. It has been investigated in previous studies that loading of higher amounts of VE in order to stabilize the bare oil rich in PUFAs is not a competent tactic, and as compared to antioxidants, it behaves as prooxidant [18,19,51]. In prior researches, the influence of VE as a prooxidant as well as an antioxidant in an emulsified system has been investigated; but this is interlinked with its entrapped amounts [52,53]. In the current study, superior oxidation level of nanoemulsions might be owing to use of greater amounts of 3% w/w VE and superior unsaturation degree of TFO.

3.1.4. Storage Stability of Vitamin-Loaded Nanoemulsions

All BC and VE enriched nanoemulsions were kept at 25 and 40 °C over 30 days of storage in order to explore the influence of storing temperatures on the retention of BC as well as of VE. A smooth declining trend in the concentration of BC was reported for all nanoemulsions except NE2 that disclosed a sharp declining trend on storage at 25 °C, and only 2.34% BC was retained over 30 days storage as depicted in Figure 4A. Loading of VE in NE4 and NE6 based on MCT provided greater BC retention around 35.17% and 33.89%, respectively, in comparison with NE2 nanoemulsion (Table 1). NEI nanoemulsions encapsulating (TFO and BC) showed the greater BC retention around 42.98% throughout storage, and further loading of VE in NE3 and NE5 nanoemulsions encapsulating (TFO and BC) reduced the BC retention. It seems that reduction in BC was reported contrarywise relational to VE concentrations. Higher amounts of 3% w/w VE resulted in a greater reduction in each oil phase, and this behavior is in accordance with our findings of oxidation as highlighted in Section 3.1.3. Although MCT showed superior oxidative stability, further assessment of BC retention explored that oxidation study is not so reliable standard to observe the stability of any system. However, further
experiments are needed to explore the real providence of bioactive. As TFO has a larger molecular structure, allowing it to hold up a higher quantity of BC, but at a similar moment, it displayed very poor solubility in the direction of oxidation that might be owing to its higher unsaturation degree. Though, in earlier research, Sharif and co-workers had reported a great BC retention loaded inside MCT and stabilized via OSA-MS. The most suitable reason for higher BC retention could be due to the usage of a higher quantity of OSA starches (>30%) to stabilize emulsions rather than the present study (2%). At 40 °C, the results of BC retention could be due to the sensitivity of BC at higher temperatures. The greater declining trend in BC loss was observed even in the occurrence of VE that might be owing to the sensitivity of TFO with respect to oxidation. As our oxidation findings of nanoemulsions also showed greater oxidation for those nanoemulsions that comprise TFO alone or combined with VE, as presented in Figure 4A,B. However, NE4 and NE6 nanoemulsions framed with MCT had displayed 34.98% and 31.22% BC retention after 30 days of storage, respectively. This behavior of MCT-based nanoemulsions indicated that the existence of VE had successfully provided protection to the BC contents, but this trend was not observed for TFO-based nanoemulsions. The VE-loaded nanoemulsions were further stored at 25 and 40 °C in order to access the VE retention. Nanoemulsions equipped with 2% w/w of VE concentrations exhibited greater VE retention at 25 °C. After 30 days of storage at 25 and 40 °C, NE4 nanoemulsion encompassing MCT showed supreme retention behavior of VE about 94.3% and 90.1%, respectively, as highlighted in Figure 4C,D. On the other hand, NE5 nanoemulsion enclosing TFO showed 88% and 79.8% at 25 and 40 °C, correspondingly. The minimum retention of VE loaded inside the TFO-based nanoemulsions could be due to the sensitivity of TFO with respect to oxidation, as covered in Section 3.1.3. Though, this study indicated superior retention for VE ~80% throughout storage at 40 °C, exhibiting that VE is less sensitive toward oxidation than BC. Our findings of greater VE retention inside the MCT-based nanoemulsions were in accordance with an earlier study [54].

Figure 2. Effect of storage conditions on MPS of vitamin-loaded nanoemulsions; (A,C) 25 °C and (B,D) 40 °C. NE1–NE12 are given codes to the produced nanoemulsions, as illustrated in Table 1. Values with different letters are significantly different (p < 0.05).
Figure 3. Oxidative stability of vitamin-loaded nanoemulsions over one month of storage at 25 °C. (A,C) peroxide value. (B,D) thiobarbituric acid reactive substances NE1–NE12 are given codes to the produced nanoemulsions, as illustrated in Table 1.

Figure 4. Changes of BC and VE encapsulated within nanoemulsions over one-month storage; (A,C) 25 °C and (B,D) 40 °C. NE1–NE12 are given codes to the produced nanoemulsions, as demonstrated in Table 1.
3.2. Effect of Cinnamaldehyde (CIN) on the Physicochemical Stability of Vitamin-Loaded Nanoemulsions

In the first section, PGU-based nanoemulsions (NE1-NE6) encapsulating TFO and MCT oil phases loaded with BC alone or in combinations with diverse levels of VE were fabricated. The physicochemical stability of fabricated nanoemulsions was evaluated, and findings of MPS and oxidation showed that loading of 3% w/w VE increased the size of particles as well as the system exhibited instability in response to oxidation. It has been investigated in the above section that loading of VE decreased and increased retention of BC in TFO-based nanoemulsions and TFO-based nanoemulsions, respectively. In the second section, 1% w/w cinnamaldehyde was used as an antioxidant in order to investigate its influence on the physicochemical stability of 0.1% w/w BC and 2% w/w VE-loaded nanoemulsions. Additionally, TW-80 was also used for the fabrication of nanoemulsions in order to shed light on a significant difference with PGU.

3.2.1. Impact of Loading Cinnamaldehyde on the Size and Z-Potential of VE-Loaded Nanoemulsions

Loading of 1% w/w CIN resulted in a decrease in MPS for PGU-based nanoemulsions covering TFO and MCT enriched with BC (NE7 and NE8), as expressed in Table 1. A declining trend in MPS by loading of CIN was observed that might be due to the lowering interfacial tension effect of CIN. After loading of CIN in PGU-based nanoemulsions (coded by NE9 and NE10) equipped with 0.1% BC and 2% VE showed intermediate MPS results in comparison with their individual encapsulation findings. However, a significant loss in MPS was noted for NE11 and NE12 (Table 1). The smallest particle size of TW-80-based nanoemulsions was previously examined instead of sodium caseinate emulsions [55]. As TW-80 is known to be the smallest molecular emulsifier that has the potent capability to lower interfacial tension among aqueous and oil phases in comparison with larger molecular emulsifiers [56]. In short, loading of CIN could not make any significant difference in terms of PDI results of TW-80 and PGU-based nanoemulsions, and values were quite lower than 0.15, as stated in Table 1. A significant loss in ZP results was observed for PGU-based nanoemulsions by loading of CIN with respect to those nanoemulsions that have no CIN. However, the findings of the current study revealed ZP values above −29, indicating potent electrostatic repulsion force among the dispersed oil particles within the aqueous suspension. TW-80-based nanoemulsions (NE11 and NE12) exhibited neutral behavior, demonstrating non-ionic characteristics of TW-80 [56].

3.2.2. Impact of Storage Conditions on MPS of BC-, VE-, and CIN-Loaded Nanoemulsions

Loading of CIN offered physical stability to the system, and even after the storage period, nanoemulsions NE7 and NE8 presented 15.2 and 36.2 nm rises in MPS at 25 and 40 °C, respectively as presented in Figure 2C,D. Overall, each nanoemulsion exhibited a superior increase in MPS that was occurred because of greater storage temperature (40 °C), and NE10 demonstrated the extreme rise in MPS around 38.3 nm. However, NE11 and NE12 nanoemulsions (Table 1) based on TW-80 were observed to be more stable rather than PGU-based nanoemulsions. TW-80 provided great stability over PGU because smaller molecular emulsifiers can adsorb more proficiently at the O/W boundary [56].

3.2.3. Impact of Loading of CIN on Oxidative Stability of BC- and VE-Loaded Nanoemulsions and Bare Carrier Oils

Numerous researches are available that oppose the “polar paradox” and recommend that the efficacy of antioxidants is based on several aspects besides the polarity, such as surface accessibility, the structure of antioxidant, splitting, relationship between emulsifier and antioxidant, and concentration [18,52,57]. Thus, we considered exploring the impact of CIN loading on oxidative stability of BC and VE-loaded nanoemulsions equipped with PGU and TW-80. Figure 3A depicts that, loading of CIN significantly reduced the POV production inside the NE7 nanoemulsions as compared to NE1, NE3, and NE5 nanoemulsions emulsified by PGU. Further, by loading CIN into NE9 and NE11, a reduction trend was observed in the case of POV production, and NE9 nanoemulsion emulsified...
by PGU showed the least production of POV over NE11 emulsified by TW-80. On the other side, loading of CIN into MCT-based nanoemulsions did not exhibit any significant difference; however, MCT-loaded nanoemulsions presented the very least production of POV. Secondary oxidation findings were in accordance with primary oxidation results in this study. However, differing from POV findings, NE9 nanoemulsion embodied with PGU presented a little bit greater TBARS results rather than NE11 emulsified with TW-80 (Figure 3B). However, an opposite trend has been observed in previous studies regarding the delivery of oxidative stability to the nanoemulsions emulsified by different emulsifiers, such as the smaller and greater molecular structure of emulsifiers. As an example, Berton and his colleagues observed greater oxidative stability for Tween-20-based nanoemulsions over proteins [58], while Kargar et al. [59] investigated different trends regarding the stability of nanoemulsions. Overall, MCT-loaded nanoemulsions showed greater oxidative stability, which was found to be more stable. Among TFO-based nanoemulsions, NE7, NE9, and NE11 nanoemulsions revealed comparatively greater stability. Though, loading of CIN alone or in mixing with BC and VE offered superior oxidative stability to the produced nanoemulsions, demonstrating its great potential as an antioxidant. Figure 3C,D openly demonstrates the impact of entrapped CIN on the oxidative stability of free oils where greater values of POV and TBARS were observed for TFO over MCT. Loading of CIN increased the oxidation level for both kinds of free oils and could not act as an antioxidant. This contradicts the behavior of CIN in free oils, and nanoemulsions appealed that lipophilic antioxidant performs well in lipid-based nanoemulsions matrices as compared to free oils that endorse the “polar paradox” mechanism.

3.2.4. Impact of CIN Loading on Retention of BC and VE

Effect of loaded CIN was accessed on the BC retention throughout storage for 30 days at 25 and 40 °C. After 30 days of storage at 25 °C, NE7 and NE8 nanoemulsions (Table 1) revealed the highest BC retention around ~52.23% and ~57.02%, respectively, as elaborated in Figure 4A. Furthermore, loading of CIN within NE9 to NE12-based nanoemulsions presented loss in BC; but TW-80-based nanoemulsions enriched with MCT oil showed more BC reduction. NE7 and NE8 nanoemulsions reserved a great amount of BC at 25 °C. An identical trend regarding BC retention was observed in NE9, NE10, NE11, and NE12 nanoemulsions at 25 °C. Though, NE9 nanoemulsion presented higher BC retention, around 42.3% over a storage period of one month at 40 °C, as stated in Figure 4B. Loading of CIN within NE10 and NE12 nanoemulsions reduced VE contents, while an opposite trend was observed regarding reduction in VE contents in NE9 and NE11 nanoemulsions at 25 °C for 30 days of storage (Figure 4C). However, there was no significant impact observed on the VE retention by any kind of emulsifier. Even at 40 °C, nanoemulsions revealed an identical trend in the case of VE retention, and NE5 nanoemulsion presented the least VE retention ~79.8%, as seen in Figure 4D. Overall, each nanoemulsion exhibited VE retention above than ~80%, and NE4 nanoemulsion presented ~90.1% VE retention rather than others over a storage period of one month at 40 °C. Antioxidants perform differently within diverse emulsified systems; however, they deliver different oxidative stability when they are used together. For instance, Qian and his team used aqueous and lipid-soluble antioxidants in single form as well as in combined form to enhance the BC stability. They reported that EDTA performed excellently in individual form as compared to VE, and their combined form offered greater stability rather than VE acetate but not higher than EDTA, signifying antagonistic potential among VE acetate and EDTA [14]. In another previous research, better VE retention was observed in whey protein isolate (WPI)-based nanoemulsions, while the defensive potential of ascorbic acid was based on molar percentages of WPI and ascorbic acid [60]. In current work, CIN significantly enhanced BC retention in all nanoemulsions covering BC and CIN, whereas it displayed intermediate consequences when entrapped within the nanoemulsions encapsulating BC, VE, and EU together (Figure 4A). Additionally, throughout storage at 40 °C, nanoemulsions encompassing a mixture of BC with VE and CIN presented to some extent greater BC retention rather than nanoemulsions holding of
BC + VE as well as BC + CIN as illustrated in Figure 4B. It is an understood phenomenon that emulsifiers could play a crucial role in the stability of nanoemulsions. As reported by Qian et al. [61] that emulsifiers such as proteins having greater molecular weight exposed a smaller amount of degradation rather than Tween-20-based nanoemulsions because of their smaller molecular weight. Mao et al. [62] fabricated BC-loaded nanoemulsions stabilized by larger and smaller molecular-based emulsifiers where they reported BC retention in flowing order protein > Tween-20 > OSA starch during the storage period. Similarly, a great BC retention of OSA-MS stabilized nanoemulsions was observed over the storage of 30 days by Liang et al. [44]. However, in this work, TW-80-based nanoemulsions showed slightly lesser BC retention that could be owing to their smaller particle size instead of PGU-based nanoemulsions. A reduction in MPS causes a rise in interfacial surface area that further upsurges the oxidation rate, resulting in a supreme loss in BC [63]. The most suitable reason for the healthier character of PGU might be owing to the OSA-MS capabilities to produce denser interfacial coatings that can protect the entrapped lipids from the aqueous phase [40].

4. Conclusions

Nanoemulsions comprising FSVs and CIN emulsified with PGU and TW-80 provided excellent physical stability over a storage period of one month at diverse temperatures. Different kinds of emulsifiers (PGU and TW-80), carrier oils (TFO and MCT), and CIN loading all directed toward prominent changes in the properties of bioactive compounds toward oxidation inside the nanoemulsions as well as within free oils. Herein, we investigated BC to be more sensitive as well as superior deprivation of VE, and BC was detected from nanoemulsions kept at 40 °C. Loading of CIN enhanced the oxidative stability and improved FSVs retention of produced nanoemulsions throughout a prolonged storage period. PGU-based nanoemulsions offered a little bit more or equivalent stability to the entrapped bioactive rather than TW-80-based nanoemulsions. Additionally, loading of CIN and VE performed dissimilar in each nanoemulsions holding dissimilar carrier oils. CIN entrapment performed being an antioxidant in each lipid phase that framed with TFO and MCT, but VE acted as an antioxidant and prooxidant in MCT and TFO, correspondingly. The changes in BC retention and oxidative stability proposed that the oxidative investigation is not enough to observe the stability of any emulsified system; however, still more studies on entrapped bioactive compounds are needed to find out the real fortune of bioactive compounds. This study could be more useful for designing oxidative stability of nano-emulsified systems in order to ensure the simultaneous incorporation of diverse lipophilic bioactive compounds as well as their application inside the food and beverage matrices.

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