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PHARMACEUTICAL FORMULATION STRATEGY APPROACH FROM RED PALM OIL (ELAEIS GUINEENSIS JACQ)

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ABSTRACT

Red palm oil (RPO) comes from the mesocarp of the palm fruit (Elaeis guineensis Jacq.) which is rich in carotenoids, vitamin E, and fatty acids. The use of RPO in pharmaceutical formulations poses challenges related to stability, oxidation susceptibility, and consumer acceptance due to its distinctive aroma and taste. To address these limitations, a variety of innovative formulation strategies, including emulsification, nanoemulsification, microencapsulation, and lipid-based systems have been researched. The RPO formulation aims to improve stability, bioavailability, and enhance therapeutic effects. Manufacturing techniques such as high-pressure homogenization, spray drying, and encapsulation of supercritical fluids have stabilized the bioactive components of RPO, minimizing oxidation, and controlling continuous release. Nanoemulsions and lipid nanoparticles have shown results in a wide range of applications from topical antioxidants to systemic drug delivery, by utilizing the synergistic effects of the lipophilic properties of RPO with other active ingredients. In addition, encapsulation technology has improved the stability of RPO storage, thereby expanding its usefulness in nutraceuticals and multivitamin supplements. This article also aims to bridge the research gap related to RPO formulation and provide insights into optimizing RPO formulations for broader benefits in health and disease management. The use of RPO in the future perspective is focused on nanotechnology formulations to improve solubility, stability, bioavailability, and support targeted and controlled drug delivery.

KEYWORDS *red palm oil, β-carotene, emulsification, microencapsulation, lipid nanoparticles, oxidative stability*

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INTRODUCTION

Red palm oil (RPO) is an oil derived from the meskoarp part of the palm fruit (Elaeis guineensis Jacq.) which is produced through the refining process of crude palm oil (CPO) either physically or chemically by retaining important compounds such as carotenoids, tocopherols, and tocotrienols that are fat-soluble (Gao et al., 2023). The RPO refining process includes degumming using phosphoric acid, neutralization using NaOH, and deodorization to remove rancid odors in the oil (Purnama et al., 2020). Red palm oil has the same properties as Refined, Bleached, and Deodorized (RBD) oil, but the difference in the refining process of RPO is that it does not go through some bleaching process and without high heating which can lead to a reduction in bioactive compounds such as carotenoids, vitamin E, and sterols. RPO has a distinctive red color because it contains high carotene compounds and low free fatty acids (C. H. Tan et al., 2021). After the RPO distillation process, the fractionation process is carried out to separate the liquid fraction (olein) and the solid fraction (stearin). RPO fractionation consists of crystallization and filtration/centrifugation or commonly called dry fractionation (Doloking et al., 2020). The results of the RPO fraction have been used and marketed commercially for red palm oil products (Nagendran et al., 2000). The downstream product and RPO fraction can be shown in Figure 1.

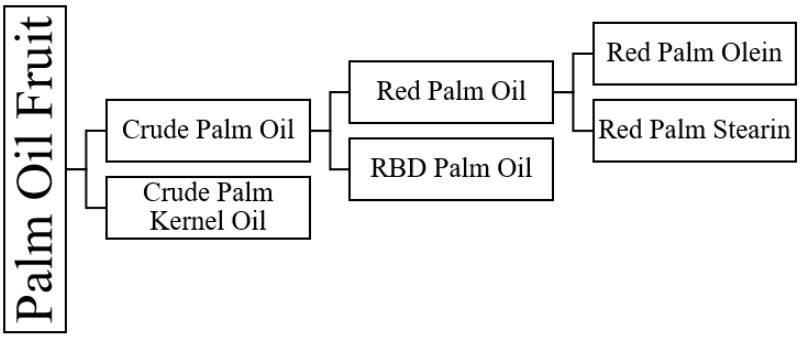

Figure 1. General Scheme Related To Downstream Products And Palm Oil Fractions

Red palm oil has several active compounds, especially carotenoid compounds that can be used as provitamin A (PVA). In addition to carotenoids, RPO also contains vitamin E which functions as a powerful antioxidant to protect cells from damage caused by free radicals (C. H. Tan et al., 2021). Both carotene and vitamin E are able to lower oxidative stress and function as a preventative of several chronic degenerative diseases (Lee et al., 2018). The provitamin A carotenoids found in RPO have been reported to have high bioaccessibility, bioavailability, and retinol equivalence compared to other oil sources such as vegetables and fruits (Y. Tan & McClements, 2021). The β-carotene content in RPO can prevent vitamin A deficiency, especially in children and pregnant women (Loganathan et al., 2017). The addition of RPO to the diet of school children three times a week for a year can significantly increase serum retinol levels (Zeba et al., 2006). Research by (Mayamol et al., 2007) shows that RPO can be used to protect malnourished children against vitamin A deficiency and eye problems. This is supported by research that shows that vitamin A supplementation has a significant relationship

with stunting in children aged 24-59 months (M. G. Putri et al., 2021). In addition to being antioxidants, provitamin A and vitamin E in RPO are beneficial for skin health (Gazali et al., 2019), and improve the immune system, the body's immunity to infections, reduce the risk of cancer by warding off free radicals, and eye problems such as cataracts (Dewandari & Sofwan, 2022). The unsaturated fat content in RPO can support heart health by reducing bad cholesterol (LDL) levels and increasing good cholesterol (HDL). RPO has a cardioprotective effect, especially in protecting the heart from ischaemic damage through mechanisms that increase nitric oxide (NO) production and activation of other signaling pathways that support heart function. Animal studies show that RPO can reduce the risk of heart tissue damage during ischemia and improve the heart's tolerance to hypoxia conditions. The antioxidant content in RPOs, such as tocotrienols and carotenoids, contributes to anti-cancer activity. Several studies have shown that RPO may reduce the side effects of chemotherapy and aid in the management of colon cancer through increased activity of detoxifying enzymes such as glutathione S-transferase (Loganathan et al., 2017).

The content of active compounds such as carotenoids and vitamin E in RPO is unstable and sensitive to oxidation when exposed to light and temperature. Degradation of these active components can cause nutrients in RPO to decrease (G. S. Putri et al., 2023). The use of RPO as a multivitamin has limitations on its storage because it is susceptible to oxidation and damage during storage, as well as lowering the bioactive content in RPO (Armetha et al., 2024). In addition to storage-related limitations, RPO also has a distinctive taste and aroma so that it is likely to be less preferred by consumers, especially children, in the formulation of food or beverage products (Loganathan et al., 2017; Narasinga Rao, 2001). RPO has hydrophobic properties that make it difficult to formulate into water-based products and require special formulation techniques in order to be used effectively in food products and pharmaceutical preparations (Sari et al., 2018). Thus, to overcome the limitations of RPO requires an innovative formulation strategy. Various formulation approach strategies to overcome RPO problems such as emulsions, nanoemulsions, Solid Lipid Nanoparticles (SLN), Nanostructured Lipid Carriers (NLC), microencapsulation, and nanoparticles have been developed to maintain stability, improve bioavailability, and the effectiveness of RPO in various applications. Thus, this review aims to examine the various formulation engineering approaches used to optimize the stability and effectiveness of red palm oil (RPO) and provide insights related to formulation strategies using RPO to optimize their effectiveness by analyzing formulation, evaluation, and release profiles in drug delivery systems. This review will also bridge the gaps in the literature by exploring the role of RPO in improving the bioavailability, sustainability, and flexibility of formulations, so that it becomes something new and relevant regarding the formulation of RPO.

RESEARCH METHOD

This study uses an experimental approach to evaluate the effectiveness of Red Palm Oil (RPO) formulations in pharmaceutical applications. RPO will be formulated using several techniques, such as emulsification, nanoemulsification, and microencapsulation, to improve the stability and bioavailability of its bioactive components. Each formulation will be analyzed through physicochemical testing,

including peroxide number and iodine value, to determine oxidative stability and final product quality.

The samples generated from the formulation technique will be evaluated using characterization methods such as particle size, distribution, and morphology using electron microscopy. In addition, the bioavailability of RPOs in different formulations will be tested through in vitro tests using controlled release models. The data obtained will be statistically analyzed to assess significant differences between each formulation.

The results of this study are expected to provide insight into the optimization of RPO formulations for nutraceuticals and pharmaceutical preparation applications, as well as bridge the existing research gap. Thus, this study aims to develop innovative formulation strategies that can improve the effectiveness and acceptance of RPO in health products and supplements.

RESULT AND DISCUSSION

Composition of Red Palm Oil

Red palm oil is extracted from the meskoarp part of the palm fruit which contains a lot of fatty acids. RPO has a balanced percentage of fatty acids which are 50% saturated fatty acids, 40% monounsaturated fatty acids, and 10% polyunsaturated fatty acids (Gao et al., 2023). This balanced fatty acid composition allows red palm oil to be more resistant to lipid oxidation than other vegetable oils that have a high monounsaturated fatty acid composition. Saturated fatty acids contained in RPO include lauric acid (C12:0), myristic acid (C14:0), palmitic acid (C16:0), and stearic acid (C18:0). Meanwhile, unsaturated fatty acids include oleic acid (C18:1) and linoleic acid (C18:2). The high content of palmitic acid in RPO (42-47%) has a neutral effect on blood cholesterol levels and does not increase cholesterol levels like other saturated fatty acids (C. H. Tan et al., 2021). The high oleic acid levels in RPO also have a structural role in cell membranes that function in signal transduction to maintain membrane moisture so that the function of LDL receptors on cell membranes is maintained. Therefore, the cholesterol intake cycle can take place faster and potentially help lower cholesterol levels (Tarigan et al., 2022).

The percentages of saturated fatty acids, monounsaturated fatty acids, and polyunsaturated fatty acids at RPO were around 41.4-47.3%, 41.5-45.9% and 10.7-12.7%, respectively. RPO has a much lower content of polyunsaturated fatty acids or PUFA (Poly Unsaturated Fatty Acid) than oil that has not been refined such as CPO. This is because components with a high melting point are separated into solid fractions or called stearine fractions during the fractionation process (Teh & Lau, 2021). Triglycerides with a low melting point fatty acid composition will separate to form an olein fraction and triglycerides with a high melting point fatty acid composition will separate to form a stearin fraction (Doloking et al., 2020). RPO also has a significantly higher diglyceride content and lower triglycerides compared to palm oil or CPO (Purnama et al., 2020). The high diglyceride composition is due to the hydrolysis process that occurs when the mesocarp is exposed to water vapor and heat prior to solvent extraction (Teh & Lau, 2021).

The fractionation results of CPO showed an increase in several constituents such as carotenoids and vitamin E due to the refining process. The concentration of carotene and vitamin E in CPO is lower compared to RPO, but fatty acids remain

at a not much different ratio (Goon et al., 2019). After fractionation, the olein fraction and stearin fraction both have high palmitic acid (C18:0) compared to other saturated fatty acids and the olein fraction has a high oleic acid content (C18:1) compared to the stearin fraction. However, the palmitic acid content in the olein fraction of RPO is slightly lower than that of the stearin fraction of RPO (Delisle, 2018). This is because during the fractionation process, RPO separates the olein and stearin fractions based on the difference in melting point where stearin will retain most of the saturated fatty acids such as palmitate so that the fatty acid content in the stearin fraction is higher than that of olein (Hasibuan, 2012; Pangestu et al., 2017).

RPO also consists of phytonutrients such as carotene, vitamin E, phytosterols, squalen, ubiquinone, and coenzyme Q10 (Purnama et al., 2020). Carotenoids are fat-soluble compounds that must be maintained during the refining process so that they do not degrade and give the RPO a red color (Loganathan et al., 2017). Total carotene in RPO is around 500-700 μg/g in 90% α-carotene and β-carotene (Delisle, 2018). Meanwhile, based on the Indonesian National Standard, it is stated that the total carotene in the RPO must be greater than 400 μg/g (BSN, 2022). About 80% of carotenoids are composed of 0.2% phytoene, 0.6% phytofluene, 41.3% α-carotene, 10.2% cis-α-carotene, 41.0% β-carotene, cis-β-carotene, 0.6% ζ-carotene, 0.8% γ-carotene, 0.8% δ-carotene, 0.2% neurosporene, 0.5% α-zearotene, 1.3% β-zeacarotene, and 1.0% lycopene. However, only α-carotene, β-carotene, and γ-carotene showed provitamin A activity (C. H. Tan et al., 2021).

In addition to carotenoids, vitamin E also contributes to the oxidative stability of RPO and as an antioxidant. Vitamin E in RPO consists of tocopherols and tocotrienols with a total concentration of vitamin E ranging from 600-1000 μg/g. Tocopherols and tocotrienols in RPO consist of 19% α-tocopherols, 29% α-tocotrienols, 41% γ-tocotrienols, and 30% are tocopherols (C. H. Tan et al., 2021). Tocopherol has activity in breaking the radical chain well. Tocopherol will release the active hydrogen from the sixth hydroxyl group on the oxanaphthalene ring, capture free radicals, and form a stable compound with a ROO- or R- group, thereby inhibiting the free radical chain (Castelo-Branco & Torres, 2009).

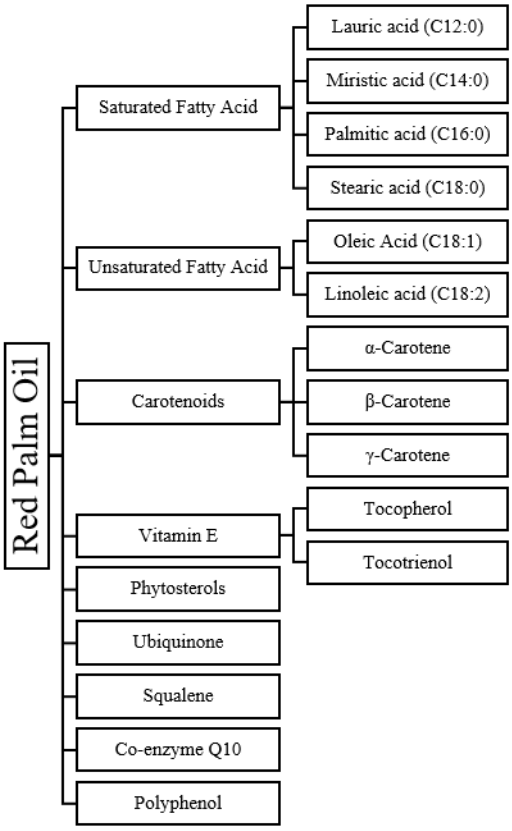

Figure 2. Constituents of *Red Palm Oil (RPO)*

Other minor phytoconstituents found in RPO are phytosterols, ubiquinones, coenzyme Q10, squalene, and polyphenols. In RPO, total phytosterols are about 325-365 µg/g, squalane 14-15 µg/g, coenzyme Q10 18-25 µg/g, ubiquinone 18-25 µg/g (Loganathan et al., 2017). Squalene is a triterpenoid compound with six double bonds and as a biogenic precursor of sterols as well as a natural source of nutrients for skin health (Nainggolan & Sinaga, 2021). Other ingredients in RPO are polyphenols which are a mixture of complex compounds including oleuropein, 4-hydroxyphenylethanol (tyrosol), 3,4-dihydroxy-phenylethanol (hydroxythyrosol), 4-hydroxyphenylacetic acid, protocatestrong acid, and citric acid and contribute to oxidative stability. The polyphenol content in RPO is around 45-50 mg/kg of total polyphenols (Alongi et al., 2022). A summary of the major and minor constituents in the RPO is shown in Figure 2. Meanwhile, the concentration of fatty acids and phytonutrients in RPO and fractionation results are shown in Table 1.

Table 1. Fatty acid and phytonutrient composition of Red Palm Oil (RPO)

References	(Delisle, 2018)	(Tan et al., 2021)	(Marliyati et al., 2021)	(Gao et al., 2023)	(Tea & Lau, 2021)	(Malaysian Standard, 2007a)	(Malaysian Standard, 2007b)
	Red Palm Oil				**PPMO**	**Palm Olein**	**Palm Stearin**
Saturated Fatty Acids							
- Lauric Acid (C12:0) (%)	0,2	-	0,12	0,22 – 4,36	2,19	0,2 – 0,4	0,1 – 0,3
- Miristic Acid (C14:0) (%)	1,0 – 1,5	-	0,61	0,90 – 2,33	1,39	0,9 – 1,2	1,1 – 1,7
- Palmitic Acid (C16:0) (%)	42,0 – 47,0	-	34,05	34,96 – 42,96	35,55	38,2 – 42,9	49,8 – 68,1
- Stearic Acid (C18:0) (%)	4,0 – 5,0	-	2,87	3,87 – 5,83	3,87	3,7 -4,8	3,9 – 5,6

References	(Delisle, 2018)	(Tan et al., 2021)	(Marliyati et al., 2021)	(Gao et al., 2023)	(Tea & Lau, 2021)	(Malaysian Standard, 2007a)	(Malaysian Standard, 2007b)
	Red Palm Oil				PPMO	Palm Olein	Palm Stearin
Unsaturated Fatty Acid							
- Oleic Acid (C18:1) (%)	37,0 – 41,0	-	36,39	38,99 – 42,27	44,99	39,8 – 43,9	20,4 – 34,4
- Linoleic Acid (C18:2) (%)	9,0 – 11,0	-	9,13	10,70 – 11,57	11,10	10,4 – 12,7	5,0 – 8,9
Total Carotenes (ppm)	500 – 700	500 – 786	220 – 237 (β-karoten)	91,48 – 154,04	1312	500 – 1200	300 – 500
Total tocopherol & tocotrienol (ppm)	600 – 1000	600 – 1000	-	327,93 – 473,43	1643	-	-
Phytosterols (ppm)	65%	325 – 365	-	388,14 – 662,96	519	-	-
Ubiquinone (ppm)	-	18 – 25	-	-	-	-	-
Co-enzyme Q10 (ppm)	-	18 – 25	-	-	-	-	-
Squalene (ppm)	-	14 – 15	-	28,05 – 52,80	401	-	-
Polyphenol (ppm)	-	-	-	45,0 – 50,0	-	-	-

Red Palm Oil Features

Before entering the formulation stage, red palm oil must have characteristics that meet quality requirements so that RPO does not quickly oxidize or reduce active components due to oxidation. Characteristics of RPO include physicochemical properties, composition of microcompounds, and fatty acids. Good RPO quality is determined by free fatty acids and moisture content (Purnama et al., 2020). The higher the level of free fatty acids, the worse the quality of RPO will be (Azeman et al., 2015). Indonesia has standardized the content of free fatty acids (calculated as palmitic acid) from the RPO, which is less than 0.5% w/w (BSN, 2022). The high increase in free fatty acid levels is caused by the high water content so that it can cause an autocatalytic hydrolysis reaction (C. H. Tan et al., 2021). High levels of free fatty acids (FFA) can act as pro-oxidants that accelerate the oxidation process (De Leonardis et al., 2016). High levels of free fatty acids can also indicate the release of fatty acids from the bonds of triglyceride molecules through hydrolysis reactions (Doloking et al., 2020). Therefore, a method of reducing free fatty acids is needed, including by deacidification or neutralization that can neutralize free fatty acids with the addition of NaOH up to an FFA level of < 0.5% (De Leonardis et al., 2016; Purnama et al., 2020; C. H. Tan et al., 2021). Another study shows that the addition of 0.1 N NaOH in the neutralization process of Red palm oil olein (RPOO) can significantly reduce FFA in the range of 0.07-0.24% (Saputra et al., 2023). The decrease in FFA levels using NaOH occurs due to the saponification reaction, where fatty acids undergo a hydrolysis reaction with alkalis or strong bases to produce sodium salts from these fatty acids (Sumarna et al., 2022).

The peroxide number (PV) is a characteristic that indicates the oxidation rate of an oil, including the RPO, and is a parameter to indicate the degree of rancidity or damage in the RPO (Sumarna et al., 2017). Rancidity in RPO is caused by an autooxidation reaction between unsaturated free fatty acids and O2 to form peroxide compounds. These peroxide compounds will form volatile compounds that can

produce scents through various chemical reactions. The lower the peroxide number, the better the quality of the RPO (Doloking et al., 2020). The increase in PV at RPO is also influenced by exposure to high temperatures above 60°C and due to the contact between oil and oxygen during storage (Maria et al., 2016). The iodine number (IV) indicates that the lower the iodine number at the RPO, the lower the quality of the oil. This is due to oxidation factors that can break double bonds on the unsaturated fatty acids that make up triglycerides (Doloking et al., 2020). The iodine number is used to measure the level of unsaturation in oil. The more unsaturated fatty acids, the form of the oil will be in the form of a liquid and vice versa if the saturated fatty acids are high, the form will be solid. In addition, a high number of iodine will affect the high melting point due to the large amount of unsaturated fatty acids in the RPO and cause a low cloud point (condition or temperature when the oil undergoes the crystallization stage) (Hasibuan, 2012). The characteristics of RPO and RPO quality requirements are shown in Table 2.

Table 2. Characteristics of Red Palm Oil (RPO) and RPO Quality Requirements

References	(Tan et al., 2021)	(Sumarna et al., 2022)	(Marliyati et al., 2021)	(BSN, 2022)	(Sumarna et al., 2017)		(Tea & Lau, 2021)
	Red Palm Oil				**Red Palm Olein**	**Red Palm Stearin**	**Refined PPMO**
Free Fatty Acid (palmitic acid) (%)	0,1	0,04 – 0,14	0,06	< 0.5	0,17 – 0,22	0,18 – 0,22	0,18
Iodine Value (g Iod/100 g	51 – 56	-	-	> 56,0	50,79 – 52,94	37,48 – 38,84	-
Peroxide Value (meq O_2/kg)	1,5	0,87	4,55	< 10	0,03 – 0,04	0,04	2,73
Water content (%)	0,4	0,19	2,23	< 0.15	0,08 – 0,13	0,09 – 0,14	-
Slip melting point (°C)	23 – 37	-	-	-	-	-	-

Emulsions and Nanoemulsions

Emulsion is a pharmaceutical preparation that is commonly formulated for active ingredients that are insoluble or immiscible in a dispersing liquid in liquid form. Emulsions are made by mixing two liquids that do not mix with each other, where the liquid is dispersed in the form of small droplets in the other liquid (Goodarzi & Zendehboudi, 2019). Emulsions generally have a particle size of about 0.1 to 100 μm. In order for the emulsion to remain stable, an emulsifying agent is needed that functions to keep the oil and water phases from separating or undergoing coagulation called surfactants. Surfactants work by occupying the interface area between the dispersed phase and its system and helping to reduce the interface voltage between phases, thereby accelerating and improving the efficiency of the emulsification process during manufacturing (Ministry of Health of the Republic of Indonesia, 2020). The development of emulsion systems is microemulsion and nanoemulsion. Microemulsions are clear and stable emulsion systems consisting of isotropic mixtures of oil, water, and surfactants, and are often added in the form of co-surfactants with a size of 20-200 nm (Ashara et al., 2014; Goon et al., 2019). Meanwhile, nanoemulsions have a smaller globule size between 1 – 100 nm and must have properties such as thermodynamically stable and have

long-term physical stability (Kale & Deore, 2017; Sakeena et al., 2011). The types of emulsions are divided into 3 based on dispersed phases: oil-in-water (O/W) when the oil phase is dispersed in the water phase, water-in-oil (W/O) when the water phase is dispersed in the oil phase (Figure 3), and double emulsions i.e. (W/OW) or (O/W/O) when the oil and water phases are dispersed in the system and form two dispersed phases (Aulton & Taylor, 2018). Surfactants with high HLB values (8-18) will form emulsions with oil-in-water (O/W) types, while surfactants with low HLB values (3-6) will form emulsions with water-in-oil (W/O) types (Ohadi et al., 2020).

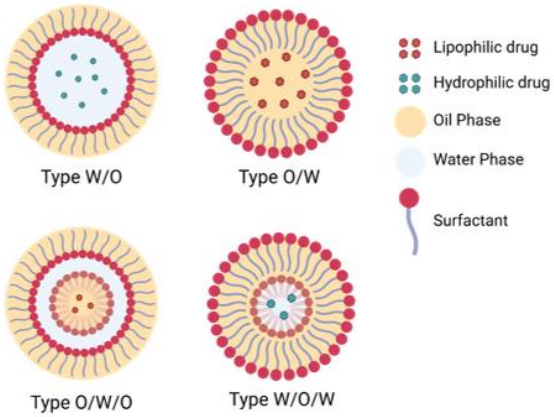

Figure 3. Types of emulsions

The advantages of emulsion preparations include mixing drugs that are hydrophobic, increasing drug absorption, increasing drug absorption topically, masking unacceptable tastes and aromas, and reducing the risk of toxicity from oils in oral use (Thakur et al., 2023). The advantages of nanoemulsions include increasing the solubility in water and bioavailability of hydrophobic drugs, as well as reducing irritation reactions in the gastrointestinal tract, keeping drugs against degradation, and reducing stability problems such as creaming, flocculation, coalization, and sedimentation (Dewandari et al., 2019; Kale & Deore, 2017). In addition, various studies related to emulsions containing lipophilic drugs can increase drug absorption in vitro and in vivo (Neves et al., 2008).

The use of red palm oil (RPO) as a multivitamin is still limited because RPO has stability limitations such as being easily oxidized so that it can cause rancidity, easily degraded to temperature and light, and has a distinctive taste and aroma that is difficult for the general public to accept. Thus, one of the strategies carried out is to formulate RPO into O/W-type emulsions because O/W-type emulsions are proven to increase the oxidative stability of lipophilic bioactive compounds (Armetha et al., 2024; Lee et al., 2018a; Narasinga Rao, 2001). Several studies have formulated RPO into O/W emulsion preparations to determine oxidative-thermal stability and investigated the kinetics of peroxide number changes during storage at different temperatures (30°C, 40°C, and 50°C) (Mursalin et al., 2014). In this study, before being made in the RPO emulsion, fractionation was carried out to obtain RPO in the form of olein and carotene content of about 1000 ppm. The emulsion was made using an oil:water ratio (7:3) with Tween 80 emulsifier (1.25%) and additives in the form of benzoate (0.2%), Butylated Hydroxytoluene (BHT) (200 ppm), Ethylenediaminetetraacetic acid (EDTA) (200 ppm), orange flavor (1.5%),

and sugar (15%). Emulsions stored at low temperatures (cooling at 9°C) have the lowest PV increase rate, which is 0.354 meq O_2/kg per week. As storage temperatures increase, the rate of PV increases as well, signaling a higher rate of oxidation. The study applied the Arrhenius model to describe the relationship between PV and temperature, suggesting that the oxidation process follows a first-order reaction, in which higher temperatures accelerate the rate of lipid oxidation. Thus, in order to extend the shelf life and minimize the oxidation of RPO emulsions, it needs to be stored in the refrigerator.

Another study developed RPO into emulsions for the characterization of RPO emulsion systems using whey protein (WP) as an emulsifier and evaluating physical stability during long-term storage as well as determining the influence of the type and concentration of WP on the stability of the emulsion (Armetha et al., 2022b). The emulsion was made using a variety of materials and concentrations of WPI, WPCa, or WPCb (2.5, 5, 10, 15%; w/v) dissolved in 0.02% (w/v) NaN3 deionized water. The RPO concentration used is 30% (w/v). The formulation techniques used are phase inversion and homogenization techniques using rotorstostators. Emulsions using WPCa and WPCb have a much lower SI value than WPI, indicating better stability. In particular, emulsions with WPCb at a concentration of 15% showed the highest stability, maintaining a Separation Index (SI) value of 0% for up to 105 days of storage. WPI-based emulsions destabilize more quickly, with separation into three layers, while WPC-based emulsions only separate into two layers (oil and serum), suggesting that WPC provides more thorough protection against RPO droplets. Emulsions with higher concentrations of whey protein (10% and 15%) are also better able to prevent the separation of oil droplets. Thus, the concentration of WPCb with a concentration of 15% is an effective emulsifier for RPO emulsion formulations.

A similar study used WP as an emulsifier in RPO emulsions to evaluate the physical stability of RPO emulsions through rheological properties (Armetha et al., 2022a). The whey-protein products used in this study are WPI90, WPC80, and WPC76 with concentrations of 2.5, 5, 10, and 15% (w/v). The emulsification process and concentration of RPO used are based on the previous method (Armetha et al., 2022b). Increased WP concentration can decrease droplet size, increase the uniformity of the emulsion, and produce a smaller ζ-potential value (-) in emulsions using WPC. All emulsions exhibit shear-thinning rheology, with the 15% WPC76 emulsion having the highest viscosity and Casson rheological constant, exhibiting the best deformation resistance. Most emulsions follow Casson's fluid model, except for the 15% emulsion WPC80 and WPC76 that correspond to the Herschel–Bulkley model. The emulsion exhibits viscoelastic characteristics with a 15% emulsion WPC76 having the highest viscoelastic range (LVE) limit (7.9%), thus reflecting superior stability to stress. The physical stability of the emulsion increased with the concentration of WP and 15% WPC76 being the most stable RPO emulsion formulation compared to other WP concentrations. Then, the use of WP was redeveloped to investigate the physical stability of RPO emulsions with different types and concentrations of WP (2.5-15% (w/v)) and using previous methods that had been used in similar studies (Armetha et al., 2024). High concentrations of WP, especially WPC76 at a concentration of 15% result in smaller droplet sizes and better stability. Emulsions stabilized with WPC show better stability compared to emulsions stabilized by WPI which indicates that WPC is

more effective in creating stable RPO emulsions. Emulsions stored at 60°C have the lowest stability, characterized by a significant increase in droplet size due to the process of protein incorporation and denaturation. The best stability is shown at a lower storage temperature of 30°C.

Several formulations of RPO emulsions continue to be developed to maximize the effectiveness of phytonutrients in RPO, such as research conducted by Agustina et al. (2021) developing an optimal formulation of β-carotene emulsions from RVPO (Red Virgin Palm Oil) using High-Pressure Homogenization (HPH) and to identify the effects of different emulsifiers (Tween 80 (12%) and CMC (3%)) and ratios to RVPO (2:1, 3:1, and 4:1) on the antioxidant activity, stability, pH, and viscosity of the emulsion. Based on the study, it was shown that formula 2 (water:oil ratio 3:1 to Tween 80) was the best formula overall, including IC50 205.95 mg/mL and AEAC (Ascorbic acid Equivalent Antioxidant Capacity) 27.02 mg Vitamin C/100 g. The emulsion with Tween 80 shows better stability and antioxidant activity compared to CMC. The HLB value of Tween 80 is more appropriate because it has a high HLB value for the type of oil-in-water emulsion needed for RVPO stabilization. Tween 80 emulsion shows a viscosity of 110 cp, so it is not easily subject to phase separation. The pH level for the Tween 80 emulsion is also stable and within the acceptable range for topical applications (5.39-5.95).

Red palm oil contains low polyunsaturated fatty acids or PUFA (Poly Unsaturated Fatty Acid) (C. H. Tan et al., 2021). Recent studies shed light on the benefits of omega-3 PUFAs in brain development and function (Innis, 2007). Thus, the combination of omega-3 PUFA and the addition of β-carotene in RPO is expected to work synergistically. Research conducted by Neves et al., (2008) combined PUFA with β-carotene formulated in a monodispersed O/W emulsion using microchannel emulsification (MC). This study investigated the effects of dispersed phase flux (Jd) and continuous phase flow velocity (Vjc) on droplet size, droplet formation behavior, and emulsion characteristics. The main goal is to improve the bioavailability and stability of β-carotene in O/W emulsions. The formula used includes β-carotene refined palm oil (45 g/L), 1% sucrose monolaurate (HLB 16), and 1% β-lactoglobulin as emulsifiers. MC emulsification uses a microchannel device where droplet formation occurs spontaneously through an interface tension mechanism. This study produced monodispersion droplets with an average diameter of 27.9 μm and a coefficient of variation (CV) of less than 4% at a lower flux level (Jd <40 L/m².hr). Monodispersion emulsions show increased bioavailability of β-carotene due to uniform droplet size and stable encapsulation and no significant degradation occurs.

In improving the stability of O/W emulsions, another strategy in the formulation of RPO emulsions is to make them in the form of emulsion powders. The research that made the emulsion powder used different emulsifier compositions, namely sodium caseinate (NaCAS) and lecithin (2.88 and 4.03%) and solid content compositions (25 and 35% (w/w)) on the physical and chemical stability of β-carotene in RPO emulsion powder (G. S. Putri et al., 2023). The main objective of the study was to evaluate the kinetics of β-carotene degradation during storage and evaluate the role of emulsifiers and solid content in maintaining emulsion stability as well as characterization of RPO emulsion powders. α-Cyclodextrin with concentrations of 12.01% and 16.82% was used to encapsulate

RPO emulsions (10.11% and 14.15%) which acted as active ingredients. The manufacture of RPO emulsion powder also uses a spray drying technique (165°C inlet and 100°C outlet) to produce a uniform and homogeneous particle size. Sodium caseinate (NaCAS) produces smaller droplet sizes, ranging from 1-30 μm, compared to lecithin, which produces droplets between 1-40 μm. The highest droplet density was observed in an emulsion with a solids content of 35% (w/w). In viscosity studies, NaCAS-based emulsions showed higher viscosity at 25% solids content (w/w) but lower viscosity at 35% (w/w) compared to lecithin-based emulsions. Lecithin-stabilized powders exhibit slightly lower moisture content compared to NaCAS, due to the lower molecular weight of lecithin, which facilitates better water evaporation during the spray drying process. The morphology of all powders shows an irregular round shape with a wrinkled surface, which is characteristic of products that are spray-dried. Regarding the β-carotene stability test, degradation follows the kinetics of the first order. Powders with lecithin showed lower degradation rates ($k = 0.018$ days^{-1} for 25% (w/w) and $k = 0.016$ days^{-1} for 35% (w/w)) compared to those using NaCAS, which had higher degradation rates ($k = 0.056$ days^{-1} for 25% (w/w) and $k = 0.048$ days^{-1} for 35% (w/w)). The study concluded that lecithin used as an emulsifier and a solid content of 35% (w/w) provided good stability for the encapsulation of β-carotene in RPO.

Nanoemulsion formulas were also developed to improve the stability of RPO. The use of a combination of emulsifiers is also used to stabilize RPO nanoemulsions in the long term and can reduce the size of droplets to nano size. Several studies have used several types and ratios of emulsifiers to the physical stability and total content of carotene in RPO nanoemulsions. The RPO and water ratios are about 2:88 (%) and the ratio of Tween 20 and Span 80 emulsifiers (% w/w) are 7:3, 3:7, 5:5, and 10:0, respectively. The manufacture of nanoemulsion uses a homogenizer at a high speed of 1200 rpm for 3 minutes and is homogenized using a high-pressure homogenizer technique (500 bar, 5 cycles). The results showed that formula III (Tween 20 and Span 80 ratio 5:5) achieved the smallest particle size compared to other formulas, namely (134.4 nm) and the lowest PDI. F3 shows better stability across temperature vairation with minimal changes in particle size and carotene content compared to other formulas that show significant degradation at 50°C due to particle agglomeration and carotenoid damage (Dewandari & Sofwan, 2022). The use of a combination of Tween 80 (HLB 15) and Span 80 (HLB 4,3) as surfactants was also used to develop stable RPO nanoemulsion formulations as well as to optimize process parameters (surfactant concentration, glycerol concentration, and homogenization pressure) to produce nanoemulsions with minimal droplet size and polydispersity index (PDI), using the Response Surface Methodology (RSM) (Chong et al., 2018). Additional ingredients such as glycerol with a concentration of 10 – 30% (w/w), RPO concentration of 20% (w/w), and citric acid 0.08% (w/w) are used for precaution. In the study, a high-pressure homogenizer homogenization technique (500-700 bar, 4 cycles) was used. The optimal formulation is composed of a surfactant of 6.09% w/w (Tween 80 = 63:37), 20% glycerol as a cosolvent and a pressure of 500 bar. The resulting nanoemulsion with a size of 119.49 nm and a PDI of 0.286 shows good stability and high retention of the active compound. The homogenization pressure and the interaction between surfactant and glycerol concentrations affect particle size and PDI. Nanoemulsions with HLB values of 11 show the most stable and show minimal changes in droplet

size after 35 days. Increased concentrations of surfactants and glycerol improve droplet size reduction and stability. The combination of surfactants improves stability compared to a single surfactant.

Another simple method of making nanoemulsions is the spontaneous emulsification method as carried out by Sari et al., (2018). The composition of surfactants is Tween 80 (40% w/w) and cosurfactants are Sorbitol (20% w/w) and varying concentrations of red palm olein (5, 10, and 15% w/w). Methylparaben (0.1% (w/w)) and propylparaben (0.02% (w/w)) as preservative. The spontaneous emulsification method occurs when aqueducts are added by titration into the oil phase mixture until a nanoemulsion is formed which is characterized by a clear liquid. Nanoemulsions with 5% RPO show the smallest particle size (67.64 nm) and retain transparency and aroma for 12 weeks. The viscosity was observed to increase gradually with storage time, associated with the effect of storage temperature on the stability of Tween 80, which can affect the interaction between particles. The pH of the formulation decreases slightly over time, while the particle size increases, likely due to the aggregation of small droplets. However, this does not result in observable instability, so the properties of the nanoscale are effectively preserved.

Apart from being an active ingredient, RPO can also be used as an excipient to dissolve and improve the stability, bioavailability, and antioxidant activity of lipophilic active compounds such as curcumin contained in curcumin (Haliza & Harimurti, 2022). The use of RPO aims to improve the stability and bioavailability of curcumin, the main bioactive compound in curcumin. The content of β-carotene and vitamin E in RPO plays a role in stabilizing curcumin and makes an additional contribution to antioxidant activity in nano-emulsion formulations. The research aims to develop a nanoemulsion formulation containing temulawak extract (Curcuma xanthorrhiza) and RPO. Using high-pressure homogenization at 1500 psi over seven cycles, the nano-emulsion was formulated with temulawak extracts (2-5%), Tween 20 (1-2%), Tween 80 (1-2%), and aquadrilles as continuous phases. The particle size ranged from 74.7 nm to 120.11 nm, with the optimal formula (5% temulawak extract, 1% Tween 80, 2% Tween 20) resulting in the smallest droplet size and highest bioaccessibility (98%). Antioxidant activity ranges from 567.69 ppm to 1324.62 ppm (AAE). The nanoemulsion was stable at 40°C, showing no significant changes in properties for five days. In vivo testing in Sprague Dawley mice showed faster elimination of curcumin from nano-emulsions compared to raw curcumin extracts.

Table 3. Summary of emulsion and nanoemulsion preparations using red palm oil (RPO)

Dosage Form	Oil	Surfactant	Co-Surfactant	Other Excipient	References
Emulsion	Refined palm oil	Sucrose monolaurate	β-lactoglobulin	-	(Neves et al., 2008)
Emulsion	RPO	Whey protein (WPI90, WPC 80, and WPC 76)	-	Sodium azide	(Armetha et al., 2022a)
Emulsion	RPO	Whey protein (WPCa, WPCb, and WPI)	-	Sodium azide	(Armetha et al., 2022b)
Emulsion	RPO	Whey protein (WPC76, WPC80, and WPI)	-	Sodium azide	(Armetha et al., 2024)

Dosage Form	Oil	Surfactant	Co-Surfactant	Other Excipient	References
Emulsion	RVPO	Tween 80	Carboxy Methyl Cellulose (CMC)	-	(Agustina et al., 2021)
Emulsion	RPO	Tween 80	-	Benzoic acid, BHT, EDTA, Orange flavor, Sugar	(Mursalin et al., 2014)
Dry Emulsion	RPO	Natrium Casseinate and Lecithin	-	α-Cyclodextrin	(Putri et al., 2023)
Nanoemulsion	RPO	Tween 80 and Span 80	Glycerol	Citric acid	(Chong et al., 2018)
Nanoemulsion	RPO	Tween 20 and Tween 80	-	-	(Haliza & Harimurti, 2022)
Nanoemulsion	RPO	Tween 20	Span 80	-	(Dewandari & Sofwan, 2022)
Nanoemulsion	RPO	Tween 80	-	-	(Yulisari et al., 2014)
Nanoemulsion	Red Palm Olein	Tween 80	Sorbitol	Methylparaben, Propylparaben	(Sari et al., 2018)

Microencapsulation and Nanoparticles

Formulation approach strategies to improve the oxidative stability of RPOs are continuously being developed. Apart from the stability of RPO, other formulation approaches are also used to mask the distinctive taste and aroma of RPO so that it can be accepted by the public. One of the strategies of the RPO formulation approach is to coat RPO using a polymer in order to control the release of active ingredients and increase the therapeutic effect called microencapsulation or encapsulation (Pratama et al., 2021). This encapsulation technology will form a membrane around the core material that can protect against light, temperature, and pH (Cheng et al., 2017). In the encapsulation of RPO into carboxymethyl sago cellulose (CMSC) beads use emulsification and vibration technology to improve oil stability, prevent oxidative degradation, and increase release into the intestine. Beads are formulated by emulsifying RPO in CMSC solution (10-15% (w/v)) with aluminum chloride as a cross-binding agent. Freeze dry is used to maintain the shape of the bead and lower the surface tension of the oil. Glycerin 1.875% (w/v) and polyethylene glycol (PEG 400) 1.875% (w/v) are used to improve bead flexibility and prevent bead shrinkage. The results of the study showed that beads made with 12.5% CMSC produced a uniform and round shape, and provided optimal encapsulation efficiency (83-96%). Beads containing PEG exhibit the best thermal stability, while glycerin improves the flexibility of the beads. Oxidative stability tests show that the encapsulated RPO has a lower peroxide value than the unencapsulated oil, which indicates increased protection against oxidation. Plasticizers will further increase stability by acting as a humectant and antioxidant (Sathasivam et al., 2018).

The increase in RPO stability occurs due to the content of carotene and vitamin E that remains protected as a result of RPO formulation in the form of microencapsulation. As done by Alfrecha & Nyam, (2018), it aims to encapsulate RPO by using co-extrusion technology to maintain carotenoid content and improve stability during storage. The composition of the encapsulation is sodium alginate (1.5% w/w) and methoxyl pectin (1.5% w/w) with a ratio of 2:1. A solution of

calcium chloride (3% w/v) with chitosan (0.1% w/v) and Tween 80 (0.1% w/v) serves as a cross-binder and hardener. The results of the study showed that the encapsulated RPO had a round shape and a smooth surface before drying, which then became fibrous and slightly irregular after drying. The drained MRPO (RPO microencapsulation) has a low moisture content (1.98%) and water activity (0.36), thereby minimizing the risk of microbial contamination. The efficiency of microencapsulation is 76.95%, due to the optimal combination of wall materials. During accelerated storage at 65°C for 24 days, MRPO was able to maintain a higher carotenoid content compared to RPO without encapsulation, although both experienced decreased antioxidant activity based on DPPH and ABTS tests. The total retention of carotenoids in MRPO remains greater until the end of the storage period, indicating more effective protection against degradation.

Another study used the spray drying method to develop microencapsulation of a mixture of RPO and flaxseed oil (FSO) to improve oxidative stability and β-carotene retention from the oil (Nayana et al., 2021). The formulation used includes a mixture of RPO:FSO (70:30 and 60:40) and whey protein isolate (WPI) and gum arabic (GA) used as a coating agent with a ratio of 1:2. The spray drying method of microcapsules produces microcapsules that are smooth and show effective encapsulation. Encapsulation showed low moisture content (2.6%) and water activity (0.46), which contributed to longer storage stability. Encapsulated β-carotene successfully retains more than 70% of its content, with an encapsulation efficiency of 40%. Encapsulates have adequate bulk density (0.335 g/mL), high solubility (60%), and good wettability.

Another method to make microencapsulation formulations is to use Solution Enhanced Dispersion by Supercritical Fluids (SEDS) without using heat or organic solvents to evaluate RPO microencapsulation as an O/W emulsion (Lee et al., 2018b). The formulations used were RPO (11.7%), water (69.9%), sodium caseinate (3.5%), maltodextrine (14%), and soy lecithin (1%). The emulsification process uses a two-stage homogenizer at 200 bar, followed by microencapsulation under optimal SEDS conditions (125 bar, 50°C, CO2 feed rate 150 L/hr). The SEDS method showed results that the microcapsules were spherical, smooth surfaces, and porous internal structures. The microencapsulation (ME) efficiency was about 92.1%, while the retention efficiency (RE) for carotene and vitamin E was about 82.7% and 94.3%, respectively. The average particle size is 5.8 μm with a small size distribution, and the moisture content is suitable for storage stability. Compared to the spray dry method, the SEDS method results in smaller particles, better surface morphology, and equivalent retention of bioactive components, but the total oil content is slightly lower.

A comparison of the SEDS method and the spray drying (SD) method in the manufacture of microencapsulation was carried out to investigate the oxidative stability, degradation conetics, and overall storage performance of bioactive components in RPO microcapsules (Lee et al., 2020). The encapsulation process involves emulsifying RPO with maltodextrine (14%), sodium caseinate (3.5%), and soy lecithin (1%), followed by high-pressure homogenization at 20 MPa over four cycles. The results of the comparison of the two methods showed that SEDS-M showed better oxidative stability with a lower total oxidation value (26.5) compared to SD-M (34.9) and unencapsulated RPO (56.7) after storage at 65°C for 35 days. The retention of bioactive compounds, including carotene and vitamin E, follows

the kinetics of first-order degradation, with SEDS-M showing higher activation energy (Ea = 36 kJ/mol for vitamin E) compared to SD-M (Ea = 29 kJ/mol for carotene), indicating better thermal protection. Morphologically, SEDS-M has a smooth spherical structure, while SD-M exhibits a wrinkled surface with a hollow center, which causes a difference in oxidative performance.

Another study also evaluated the effect of β-carotene-enriched RPO encapsulation using various combinations of coating materials on the characteristics of microencapsulation produced through spray drying. The coating materials used are maltodextrin (MD) (17.5-25%), xanthan gum (XG) (0.3-0.4%), gum arabic (GA) (2.5-7.5%), and sodium caseinate (SC) (2.5-7.5%) in different ratios, with RPO and Tween 80 as core and emulsifying materials. The results of RPO microencapsulation showed that the combination of MD with a ratio of 99.7:0.3% resulted in the highest encapsulation efficiency (72.05%), β-carotene retention (72.65%), and low surface oil content (1.03%). Encapsulation made of pure MD has a smooth surface, while formulations with MD show significant surface cracking and higher surface oil content due to weak wall material integrity. This encapsulate exhibits high water solubility (91.63–97.35%), with the MD formulation superior in terms of good wettability and lower levels of hydrophobicity compared to other combinations. Encapsulation stability and β-carotene retention are closely related to low surface oil content, confirming the effectiveness of protection from the MD combination (Yulisari et al., 2016).

Nanoparticles (NP) are also one of the strategies carried out to improve the oxidative stability of RPO. Generally, nanoparticles are made using zinc oxide (ZnO) which is included in the category of "generally recognized as safe (GRAS)" and has shown the ability as a coating to increase the stability of bioactive components (Anjum et al., 2021). This is due to ZnO's ability to block UV rays, its high antioxidant activity, so that it can prevent lipid peroxidation (Meydan et al., 2022). Thus, the advantages of ZnO as a nanoparticle coating material are utilized to evaluate the stability, physicochemical properties, and rheological properties of a multiphase system consisting of RPO and water, which are stabilized using ZnO nanoparticles (Listiarini et al., 2024). The formula used in this study was 40-90% (v/v) and ZnO (0.5-1.5% (w/v). The multiphase system is created using rotor homogenization at 18,000 rpm, with the homogenization session divided into several intervals to prevent overheating and maintain uniformity. The results showed that a multiphase system with 60-70% RPO stabilized by ZnO NP had optimal physical and chemical stability, without showing synergies or phase separation after 14 days of storage. Formulations with 70% RPO and 1.5% ZnO NP produce the most stable NPs, effectively preventing lipid oxidation and lowering peroxide (PV) values and levels of thiobinturic acid reactive substances (TBARS). The system also maintains a high carotenoid content, demonstrating ZnO's role as a physical barrier and free radical cleaner. In terms of rheology, all multiphase systems exhibit non-Newtonian characteristics with sliding thinning behavior, where ZnO concentrations show a positive relationship with viscosity and viscoelastic properties.

Solid Lipid Nanoparticle (SLN) Dan Nanostructured Lipid Carriers (NLC)

Lipid-based formulations are also developed to keep the active components in RPO stable, increase bioavailability, and can reduce toxicity and improve therapeutic effects. One of the lipid-based formulation strategies is Solid Lipid

Nanoparticle (SLN) and Nanostructured Lipid Carriers (NLC) (Viegas et al., 2023). SLN is a first-generation lipid formulation of lipid nanoparticles made from physiological lipids and can be dispersed in aqueous media or other water-based surfactant solutions (Faiz et al., 2023). SLN consists of a solid lipid core matrix stabilized using an emulsifier and is submicron in size (50 – 1000 nm) (Plyduang et al., 2022; Rodenak-Kladniew et al., 2023). The lipid phase of SLN is generally from steroids, diglycerides, or triglycerides, a mixture of glycerides, or waxes, at a concentration of 0.1 – 30 % (w/v) and remains in a solid phase at room temperature and body temperature. The concentration of surfactants used in SLN is around 0.5 – 5% (w/v) and a combination of surfactants is often used to increase the stability of SLN (Viegas et al., 2023). The advantages of SLN using solid lipids include good biocompatibility, low toxicity, good stability, and good release control of encapsulated drugs (Faiz et al., 2023).

The use of SLN has been used as a formulation of nanoparticle creams containing red palm extract (Plyduang et al., 2022). The study was conducted to develop day creams and night creams containing red palm fruit extract encapsulated into SLN and assess physical stability, antioxidant properties, and anti-aging effectiveness clinically. The composition used in the formulation of SLN includes Span 80 (1.12%), Tween 80 (0.83%), Glyceryl monostearate (0.30%), and 6% red palm fruit extract. The results of SLN characterization show that SLN has a size of about 600 nm with a PDI of 0.22 and zeta of -28.3 mV and is stable during the storage period at 4°C for 6 months. Then, 50% w/w SLN is formulated into the day cream preparation with the addition of sunscreen and emollient agents to the night cream. Using the high-shear homogenization emulsification method, it produces a cream that is stable during storage at 30°C for 6 months and has a pH value of 4.7 – 5.75 which is suitable for skin care applications. SLN retains high levels of tocopherol, tocotrienol, and β-carotene, providing significant antioxidant activity (49.96 μg/mL). Clinical testing on healthy female volunteers for 30 days showed improved skin hydration, elasticity, reduction in transepidermal water loss (TEWL), and decreased wrinkle depth, with both creams being well tolerated and non-irritating. The high satisfaction score (≥90%) of the participants further strengthened the level of effectiveness.

However, SLN has several limitations, namely a small drug loading capacity and the risk of drug leakage. Therefore, the researchers developed a second-generation lipid-based nanoparticle, namely NLC (Faiz et al., 2023). NLC is a lipid carrier consisting of a mixture of solid lipids and liquid lipids and the water phase consists of surfactants. The lipids used in the NLC formulation must be biocompatible so as not to pose a toxic risk in the body (Gordillo-Galeano & Mora-Huertas, 2018). The mixing of liquid lipids into the solid lipid core results in low crystallinity, improves drug storage stability, drug loading capacity, and encapsulation efficiency, and has controlled release. In addition, NLC is able to encapsulate hydrophobic and hydrophilic compounds and is made from ingredients that are generally considered safe (GRAS) by the Food and Drug Administration (FDA) in the United States (Rodenak-Kladniew et al., 2023). The advantages of NLC as a carrier system include having a high drug load capacity, either hydrophilic or lipophilic drugs, minimizing the risk of drug leakage, high drug and nanoparticle stability, can increase oral bioavailability, and facilitate the delivery of anti-cancer drugs to target cells (Faiz et al., 2023; Rawal et al., 2023).

Red palm oil consists of a solid fraction and a liquid fraction where the fractionation results can be used in the formulation of NLC. The utilization of olein and stearin can be formulated into NLC formulations to formulate and characterize NLC-RPO using the microemulsion method reviewed from the stability and efficiency of encapsulation (Elianarni et al., 2023). The optimal formulation in the study was with a ratio of Tween 80:Span 20 (80:20), lipid:surfactant (1:4), palm stearin (PS):RPO (6:4) resulting in a particle size of 24.73 nm, zeta potential -7.43 mV, PDI 0.06, and encapsulation efficiency of 99.57%. NLC is stable for 30 days at room temperature, showing minimal increase in particle size. Other studies have also used palm stearin as a composition of NLC for formulation and characterization of NLC using RPO and stearin for potential evaluation as a drug delivery system. NLC was created using the heat homogenization method, in which RPO and PS were melted at 60°C, mixed with Tween 80 surfactant and water. The 5:5 ratio of RPO results in the most stable NLC, with a turbidity of 1.002%, a transmittance of 12.943%, a viscosity of 24.67 dPa.s, a β-carotene content of 80.5 ppm, a color brightness of 40.11, and a hue value of 77.74, indicating a reddish-yellow color. These properties are due to the compatibility between RPO and PS, both derived from crude palm oil, and the stabilizing effect of Tween 80. An increase in RPO levels is related to an increase in viscosity, which is caused by the presence of liquid lipids that affect the interaction between particles in the carrier matrix. The concentration of β-carotene also increased with high RPO levels, where the ratio of 5:5 resulted in the highest concentration (80.5 ppm), thereby increasing the potential antioxidant capacity of NLC. This study concludes that RPO and PS can be efficiently formulated to produce stable NLCs with high β-carotene content and can be used in functional food systems (Redha et al., 2023).

CONCLUSION

Red palm oil (RPO) which is rich in β-carotene, vitamin E, and essential fatty acids has significant potential and is formulated by various methods such as emulsification, nanoemulsification, microencapsulation, and lipid nanoparticles. Future strategies for RPO focus on leveraging nanotechnology to improve solubility, stability, and bioavailability through nanoemulsions, liposomes, or solid lipid nanoparticles, enabling targeted and controlled drug delivery. Topical and transdermal RPO applications, such as in wound healing and anti-aging products, show good antioxidant and anti-inflammatory properties for skin health. For oral administration, soft gel capsules, and controlled release systems can improve bioavailability and therapeutic effects, especially in addressing cardiovascular and neurological health.

In addition, the role of RPO in nutraceuticals, such as functional foods and micronutrient delivery systems, offers a promising approach to addressing nutrient deficiencies such as vitamin A deficiency in developing regions. The combination of RPO with other drugs or natural compounds provides an opportunity to create synergistic effects in anti-inflammatory, anti-cancer, and anti-microbial therapies. On the other hand, the use of RPO as an excipient can help improve drug solubility while amplifying the therapeutic effects of drugs. In order to be widely accepted, standardization and quality monitoring of RPO formulations are needed, accompanied by measures to make these formulations more economical and accessible. By integrating advanced technology, sustainable practices, and

innovative delivery systems, RPO can become the cornerstone of the future of pharmaceutical and nutraceutical applications.

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