Cocoa Butter: Evolution from Natural Food Ingredient to Pharmaceutical Excipient and Drug Delivery System

Authors

Ying Hui Loke[1], Hiu Ching Phang[1], Najwa Mohamad[1], Phei Er Kee[2], Yik-Ling Chew[3], Siew-Keah Lee[4], Choon Fu Goh[5], Chien Ing Yeo[6], Kai Bin Liew[1]

Affiliations

1 Faculty of Pharmacy, University of Cyberjaya, Cyberjaya, Selangor, Malaysia
2 Biorefinery and Bioprocessing Engineering Laboratory, Department of Chemical Engineering and Materials Science, Yuan Ze University, Taoyuan, Taiwan
3 Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, UCSI University, Kuala Lumpur, Malaysia
4 M. Kandiah Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman, Kajang, Selangor, Malaysia
5 Discipline of Pharmaceutical Technology, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Pulau Pinang, 11800, Malaysia
6 Sunway Biofunctional Molecules Discovery Centre, School of Medical and Life Sciences, Sunway University, Malaysia

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Correspondence

Associate Professor Ts. Dr. Kai Bin Liew, PhD
Faculty of Pharmacy, University of Cyberjaya, Persiaran Bestari Cyber 11, 63000 Cyberjaya, Selangor, Malaysia
Phone: + 60174695260
liewkaibin@cyberjaya.edu.my

ABSTRACT

For decades, cocoa butter has been extensively used in food industries, particularly in the production of chocolate confectioneries. The composition of fats within cocoa butter, such as stearic acid, palmitic acid, and oleic acid, determines its properties. Studies have indicated the existence of at least six polymorphic forms of cocoa butter, each possessing distinct characteristics and melting points. Recently, cocoa butter has garnered attention for its potential as a delivery system for pharmaceutical products. This review thoroughly explores cocoa butter, encompassing its production process, composition, properties, and polymorphism. It delves into its diverse applications across various industries including food, cosmetics, and pharmaceuticals. Additionally, the review investigates cocoa butter alternatives aiming to substitute cocoa butter and their roles in different drug delivery systems. The unique properties of cocoa butter have sparked interest in pharmaceutical industries, particularly since its introduction as a drug delivery system and excipient. This has prompted researchers and industry stakeholders to explore novel formulations and delivery methods, thereby expanding the range of options available to consumers in the pharmaceutical market.

Introduction

The discovery of cocoa beans has made them popular for decades. Cocoa butter is the fatty seed found inside a cocoa pod, a fruit of the *Theobroma cacao* plant. *T. cacao* is a kind of small tree that grows naturally in the lowest areas of the Amazon basin's evergreen rainforest [1]. Cocoa butter has the scientific name *Theobroma cacao* L., as well as other scientific names such as *Theobroma pentagonum* Bernoulli and *Theobroma sativum* (Aubl.) Lign & Le Bey. It belongs to the domain Eukaryota under the kingdom of Plantae. More specifically, *T. cacao* L. is part of the subkingdom Tracheobionta, superdivision Spermatophyta, division Magnoliophyta, and further classified under the phylum Spermatophyta. It is categorized in the order Malvales and is a member of the family Malvaceae in the genus of *Theobroma* [2]. Therefore, the complete botanical designation for the source of cocoa butter is *Theobroma cacao* L., from the family Malvaceae. The origin of this tree is from tropical rainforest areas of Central and South America. The raw materials used to produce chocolate, cocoa, and cocoa butter are from the seeds of *T. cacao* plant. Following harvesting, the cocoa fruit is cracked to obtain the seed, then the pulp and seeds are separated by fermentation. The pulp is used in distilleries and the seeds are used to prepare cocoa powder, chocolate, and cocoa butter [3]. The naturally stable fat known as cocoa butter is sourced from the cocoa bean of *T. cacao*. It solidifies at room temperature but melts to liquid at human body temperature. Thus, it has been widely used in different industries for many years. It has been commonly used as a food flavoring, a cosmetics additive, and in food biotechnology [4–6].

Natural products serve as a fundamental foundation for the manufacturing of materials needed in different industries including the food, pharmaceutical, and cosmetic industries. However, there are some disadvantages when utilizing natural products as the source of raw materials. For example, instability and uncertainty in the yield and production of natural products. Thus, a change in strategic approaches to material production is required due to the growing population-related resource demand, growing areas becoming less viable due to environmental degradation, and extinction of plants because of climate change [7]. A review paper by Applequist et al. discussed the impact of climate change on medicinal plants. Medicinal plants contribute a lot to human health. They constitute the main component for citizens of most developing countries and the number of its consumers are increasing in wealthier countries [8–10]. To assure economic efficiency and the widespread use of limited raw materials with high added value, a variety of advanced innovative technologies have been developed to substitute natural products in order to address the issue at hand [11, 12]. *T. cacao* plants are used to produce cocoa butter, which is a value-added product employed in the processing of cocoa beans. High levels of saturated fatty acids and low levels of highly unsaturated fatty acids make up the majority of ingredients in cocoa butter, while the composition is totally dependent on plant variety and the culture circumstances. In other words, cocoa butter originating from different countries contains different compositions of saturated and unsaturated fatty acids [13]. The condition of increasing demand and supply shortages leads to an increasing interest in cocoa butter alternatives. Numerous approaches have been tried to combine various fats from exotic plants with palm oil to formulate compounds with a similar lipid composition to cocoa butter [5]. Nowadays, cocoa butter has been utilized extensively in industries other than the food industry, such as the pharmaceutical industry and cosmetics industry. Thus, this review aims to comprehensively discuss and explore the different aspects of cocoa butter, focusing on its characteristics, uniqueness, applications, and emerging uses in various industries.

Research Methodology

The key word “cocoa butter” was searched in Google Scholar and related articles were referred to and reviewed.

Production of Cocoa Butter

The production of cocoa butter starts with the removal of pulp and cocoa beans, and discarding rind. The pods are opened to reveal the beans. Then, the pods with detached rinds are placed in trays or heaps to undergo sweating and fermenting. At this step, natural liquefying enzymes present in the pulp are applied to dissolve the pulp. This process is referred to as liquefaction of the pulp, which helps to separate the bean from the pulp in an easy way. For the purposes of storage and transportation, conventional or unconventional heat sources are utilized to remove excess moisture from the separated beans. After being cleansed to get rid of unwanted materials, the dried beans are roasted under carefully monitored conditions. This procedure produces a proper chocolate flavor. The roasted beans are cracked to remove the shell. After being cracked, the beans go through a winnowing process, in which a gentle airflow is used to deshell them. The deshelled and cleaned nibs obtained are ground to produce the liquor or cocoa mass. Cocoa liquor can be directly used or blended with other ingredients for chocolate making [3].

Cocoa liquor is the primary source that is used to extract cocoa butter in the absence of other resources. Several approaches have been used to extract cocoa butter from the cocoa mass. For example, mechanical press, supercritical fluid extraction (SFE), hydraulic press, and solvent extraction are some of the examples of methods used [3]. According to Asep et al., SFE is a technique using carbon dioxide as a solvent and offers an excellent option for chemical solvents when it comes to the removal of cocoa butter from various plant matrices. SFE offers multiple essentials over current conventional techniques, most notably the capacity to generate products that are completely free of processing residues. SFE is also an alternative option that is time-saving and friendly to the environment [14]. Thus, SFE would be the best method for food grade application from the methods mentioned above [3].

Composition of Cocoa Butter

A blend of unsaturated and saturated fatty acids makes up cocoa butter. A high proportion of highly saturated fatty acids and a low proportion of highly unsaturated fatty acids can be found as the main components of cocoa butter [5]. Jahurul et al. suggested that there are three major triglycerides that contribute 92–96% of the total lipid content of cocoa butter, including glycerol-1,3-dipalmitate-2-oleate (POP), glycerol-1-palmitate-2-oleate-3stearate (POS), and glycerol-1,3-distearate-2-oleate (SOS). Out of these three triglycerides, POS occupies the greatest proportion, with a range of 42.5–46.4% yield, followed by SOS (27.8–33.0%) and POP (18.9–22.6%). Besides triglycerides, there are other components such as fatty acids present in cocoa butter, which include palmitic acid (C_{16}) 25–33.7%, stearic acid ($C_{18:0}$) 33.7–40.2%, oleic acid ($C_{18:1}$) 26.3–35%, and linoleic acid ($C_{18:2}$) 1.7–3%. The various types of fatty acids found in cocoa butter contribute about 98% of total fatty acids [13]. In a study conducted by Erickson et al., several types of vitamin E, including α-tocopherol, β-tocopherol, and γ-tocopherol, were found in cocoa butter. The amount of β-tocopherol is higher, which is followed by α-tocopherol and γ-tocopherol [15].

Properties of Cocoa Butter

The composition of triglycerides present in cocoa butter determines its properties. Cocoa butter starts to melt at a temperate range of 27 to 35 °C. Cocoa butter remains in a solid state at room temperature, and it is hard and brittle, whereas its hardness depends on the solid fat content. The hardness of cocoa butter is also affected by the nature of crystalline lattice [3].

Different countries of origin result in variation between cocoa butter in terms of composition. Asian cocoa butters tend to have higher levels of stearic acid and a lower palmitic acid content than African cocoa butters, resulting in higher SOS/POP ratios. Comparing cocoa butter from other regions, South American cocoa butters typically contain higher unsaturated fatty acid levels, which lead to higher stearic-oleic-oleic triglycerides (SOO) (palmitic acid, stearic acid, arachidic acid, and oleic acid) levels and softer cocoa butter. The melting characteristics of cocoa butters are altered by the variations in triglyceride makeup. In general, SOS melts at a higher temperature than POS, which, in turn, melts at a higher temperature than POP. In summary, Asian cocoa butters contain higher SOS, and POS has a higher solid fat content when compared to West African or South American cocoa butters. Triglycerides with larger percentages of unsaturated fatty acids melt at a lower temperature. Generally, cocoa butters produced from South American have smaller percentages of lower solid fat content than that of Asian or West African cocoa butters [16].

Polymorphism of Cocoa Butter

Polymorphism is defined as the ability of a substance to display different structures. Cocoa butter has at least six distinct structures or crystal forms. Variations in the structures or crystal forms result in different molecular arrangements and thus influence the properties of cocoa butter in different states. Cocoa butter exhibits six totally different crystal polymorphic forms with varying melting temperatures and complex crystallization behavior [17]. The Wille and Lutton nomenclature is the most frequently used nomenclature for cocoa butter polymorphism. ▶ **Table 1** shows the melting point of each form from the Wille and Lutton nomenclature, which was adapted from Quing et al. [4]. According to this nomenclature, form IV is the most stable form, with a melting point of 36 °C, whereas form I is the least stable form, melting at 16–18 °C. On the other hand, form V cocoa butter is the more desirable variety since it is also stable and more visually appealing, with a shiny smooth texture. Along with that, form V cocoa butter has a lower melting point, which enables it to melt more quickly in the mouth, than form VI cocoa butter. Tempering is a commonly used method to pre-crystallize form V cocoa butter. However, it will gradually evolve into form VI, with a higher melting point and stability over time. Form IV cannot be made on its own but slowly develops from form V [4, 18, 19].

▶ **Table 1** Melting points of cocoa butter for each form from the Wille and Lutton nomenclature [4].

Polymorphism form	Melting point (°C)
I	17.3
II	13.3
III	25.5
IV	27.3
V	33.8
VI	36.3

Applications of Cocoa Butter in Various Industries

Food industry

Cocoa butter is the main ingredient in the manufacturing of confectionery products such as chocolate making. It is a pale yellow liquid with a unique aroma and chocolate taste. It is significant and the only continuous fat phase that aids in the dispersion of other ingredients in chocolate [3, 20]. The role of cocoa butter in chocolate making includes providing texture, flavor, and mouthfeel. Cocoa butter has a melting point 27 to 35 °C. The composition in cocoa butter consists of palmitic, stearate, and oleic fatty acids, giving it a smooth melting texture when consumed. In a previous study, the researchers compared cocoa butter and cocoa butter alternatives in chocolate making. The study indicated that cocoa butter substitutes (CBSs) are more acceptable than cocoa butter replacers (CBRs) and cocoa butter equivalents (CBEs) in chocolate making among cocoa butter alternative (CBA) subgroups. The reasons that the use of CBRs and CBEs are not as preferable as CBSs in chocolate making has been studied and is stated in ▶ **Table 2** [21, 22].

Other than confectionery products, cocoa butter is also widely used for baking. The addition of cocoa butter in cakes, biscuits, pastries, and cookies aims to add richness and moisture to the products. A study done by Quek et al. titled "Effects of Cocoa Butter and Cocoa Butter Equivalent in a Chocolate Confectionery on Human Blood Triglycerides, Glucose and Insulin" aimed to evaluate and conduct research on the effects of sal fat and cocoa butter, which have comparable chemical structures, on lipidemia, insulinemia, and postprandial glycemia. Nineteen male participants in good health fulfilled the inclusion criteria and were included in the study. The researchers concluded that when compared to a brownie made with cocoa butter and SAL seed oil (SL), the brownie made with cocoa butter oleogel (CBOG) and SAL seed oleogel (SLOG) had a significantly smaller increase in plasma insulin and triglycerides. The study's findings also demonstrated that there is no difference in metabolic effects between cocoa butter and SL, and between CBOG and SLOG. This circumstance points out that Sal fat may be a suitable replacement for cocoa fat in the production of chocolate confectioneries. Additionally, the results demonstrated that their metabolic reaction is the same. Thus, there is no threat to the public's health when SAL seed and cocoa butter are "interchanged" [23].

Cosmetic industry

The functions of cocoa butter are not only limited to the food industry. It is also widely used in the cosmetics industry due to its nourishing and thickening properties. The application of cocoa butter in skincare products proved that cocoa butter provides numerous benefits to the skin, including moisturizing, aiding in skin hydration, anti-inflammatory effects, and others. According to Naik and Kumar, cocoa butter made from starch and palmitic acid contains a high proportion of saturated fat and trace amounts of

▶ **Table 2** Limitation in the use of cocoa butter replacers (CBRs) and cocoa butter equivalents (CBEs) in the production of chocolate [21, 22].

Factors	CBRs	CBEs
Melting point (cocoa butter: 35 °C)	Average melting point: > 38 °C. The chocolate bar's character becomes firm at this state, thus rendering it difficult to melt in the mouth.	Average melting point: 18.5 ± 21.78 °C. Its stability varies due to its wide temperature range.
Mixing	It can only be combined with cocoa butter in extremely small quantities.	It cannot be mixed in any ratio.
Impurity compound	Elaidic acid (E)	Diglycerides, diacyl-glycerol (DAG)
The availability of raw materials	Groundnut oil and hydrogenated oil can be found in great abundance. However, they have not been developed to be as efficient as possible.	Shea butter, kokum butter, illipe butter, and sal fat. They are quite rare.
Taste	Cocoa butter has a variable taste in which other tastes occasionally come up. This condition might be affected by the fatty acids' origin.	
Flavor	Chocolate-based products usually have an erratic taste. In addition, other flavors still appear.	

theobromine and caffeine. Additionally, it has fat-soluble antioxidants such as vitamin E in the forms of *β*-, *α*-, and *γ*- tocopherol. Cocoa butter is commonly used in the formulations of skincare products such as lotions, moisturizers, lip balms, hand creams, sunscreens, and others because of its antioxidant and hydrating features, which exert an antiaging effect [3].

Our skin works through various mechanisms to keep skin healthy and intact. Gyedu-Akoto et al. mentioned that the maintenance of skin health is significantly affected by natural moisturizing factors (NMFs) or substances that replicate the structure and function of healthy skin. While oil and fat components produced by the skin act as lubricants to moisturize the skin's surface and prevent evaporation, the condition of skin will be affected when lipid and NMF content is reduced. Surface roughness, flaking, fine wrinkles, and an unpleasant tight feeling may appear on the affected skin [24–26]. Gasser et al. compared the effects of cocoa polyphenols and cocoa butter on the skin. The study concluded that the application of cocoa polyphenols for at least 5 days can improve the structure of skin. On the other hand, it takes cocoa butter at least 12 days to exhibit the same activity. When coupled with cocoa butter, the most *ex vivo* metrics related to skin elasticity and tone are enhanced at a dose of 0.5 to 0.75 % by cocoa polyphenols. Improvement in the overall morphology of the skin as well as the expression of type I and type IV collagen and glycosaminoglycans (GAGs) on the skin were observed when cocoa butter was paired with cocoa polyphenols to be applied on the skin [27].

Monounsaturated free fatty acids (FFAs) such as oleic acid are present abundantly in cocoa butter. Monounsaturated FFAs may disrupt the skin barrier and thus act as permeability enhancers [28]. Cocoa butter is one type of fat that can prevent evaporation on the skin and provides lubrication for the skin surface. Thus, the lipid content of the skin can be maintained and result in a good texture of the skin [24, 29]. Many cosmetic products use cocoa butter as a raw material. However, one study found that it is rare to find products that use cocoa butter as a raw material for solid perfume. A study done by Septiyanti et al. investigated solid perfume made by mixing a wax base, carrier oil, and essential oil as fragrances followed a heating process. Several concentrations of cocoa butter for solid perfume were tested and optimized in this study. The outcomes revealed that the features of the finished products were remarkably impacted by the concentration of cocoa butter. Due to the absence of any new chemical groups in the finished products, the researchers involved stated that the production procedure merely involved physical processes that do not have an impact on the stability of the products. According to the results of an organoleptic test, the product with a 30 % cocoa butter concentration was chosen as the optimum formulation [29].

Pharmaceutical industry

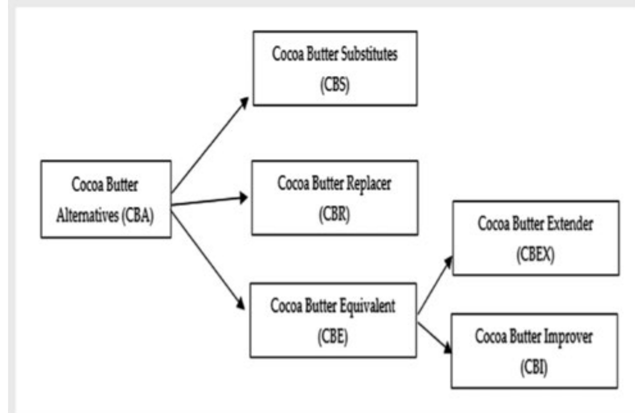
The characteristics and polymorphisms of cocoa butter have attracted the attention of researchers in the field of the pharmaceutical industry. Cocoa butter has been utilized in the development of a drug delivery system. A review published by Ramos-de-la-Peña et al. [30] suggested that cocoa butter had been studied at the nanoscale, and this is a major advance in the development of nano-delivery systems. Besides pharmaceutical products, these nanostructures can encapsulate different compounds used in the food industry, too, including food-drug ingredients, antimicrobials, vitamin, antioxidants, flavorings, and drugs. A readily available core and a protective physicochemical wall or shell constitute a nanocarrier. They have been aimed for applications of targeted delivery as well as controlled delivery of bioactive ingredients and drugs. Lipid-based systems and biopolymers (protein and polysaccharides) are the two categories of a nano-delivery system. The characteristics of carbohydrate and protein networks make them impossible to precisely control thermal and chemical process during manufacturing processes. Thus, this condition limits their use at industrial scales. Lipids have demonstrated that they are more efficient in encapsulating for large-scale productions [30]. Polymorphic transition in solid lipid nanoparticles (SLNs) depended on multiple factors and variables in the study. For instance, the uses of lipid(s) and emulsifiers generated particle size and the applied temperature during cooling and storage might exert an effect on the polymorphic transition in SLNs

[31, 32]. As per Ramos-de-la-Peña et al. [30], the solid lipid portion of SLNs is often where cocoa butter resides. Examples include when the bioactive ingredient and the heated emulsifier solution are mixed with melted cocoa butter and other fats [30, 32].

Furthermore, nano-drug delivery systems have become another important drug delivery method in cancer therapy. According to Chavda et al., the role of lipid in lipid-based nanoparticles act as penetration enhancers of the drug, thus enhancing drug solubility and diffusion from the lymphatic to the circulatory system. Food-grade lipids such as cocoa butter and olive oil have been used to synthesize cardamom essential oil (CEO)-loaded nanostructured lipid carriers (NLCs). This modification results in a small size, improved loading capacity, and provides good physical and chemical stability [33, 34]. Moreover, a review article titled "Applications of Novel Drug Delivery Systems for Enhancement Bioavailability of Antiretrovirals with Special Focus on Nanotechnology" discussed the employment of nanotechnology in antiretroviral therapy. Several drugs such as saquinavir, stavudine, and delavirdine were prepared using cocoa butter and tripalmitin as a polymer-based nanocarrier system to increase the permeability of drugs across the blood-brain barrier [35].

Another article published by Quing et al. stated the use of cocoa butter as a novel excipient for oral tablets. Research has been done on the development of fast melt tablets (FMTs) without any active components by employing the freeze-casting technique, with sucralose and cocoa powder as excipients [4, 36]. Moreover, cocoa butter is a fat that can act as a lubricant in tablet formulations. A study done by Adeagbo and Alebiowu compared the lubricating properties of cocoa butter. The cocoa butter that was co-processed with magnesium stearate and talc (CMT) had an impact on the mechanical properties of the tablets, as reflected by their tensile strength (T) and brittle fracture index (BFI). Tablets containing CMT had lower T and BFI values than tablets containing talc and magnesium stearate (MT). The findings indicated that although CMT lowered the granules' plasticity, it improved their flow rate and contributed to formulating tablets with a lower risk to cap or laminate. This study concluded that cocoa butter is easily accessible and a reasonably priced lipid that can be co-processed with a magnesium stearate/talc mixture to effectively lubricate granules. It may also be useful in reducing the risk of lamination and capping in formulations [37]. According to Quing et al., there were researchers that studied and developed a palatable medicated chocolate to deliver salbutamol and ambroxol for pediatric care. The chocolate-based formulation exhibited stability, good therapeutic efficacy, and a huge preference [4].

As time progresses, technologies undergo exceptional levels of advancement. Three-dimensional (3D) printing has been developed and now its applications can be found in our daily life. Using digital designs as a starting point, 3D printing is an additive manufacturing technique that creates an actual substance layer-by-layer. This technique had been used to print chocolate. Chocolate possesses the characteristics of melting at a predetermined temperature and solidifies quickly when it sticks to the layer before it. This is a crucial characteristic to be focused on when selecting materials used for 3D printing [38]. Hence, cocoa butter is often utilized as the "ink" for production of the 3D printing of chocolate. After printing, the chocolate obtained does not need any other process, which makes for an easier and shorter manufacturing process [39].



▸ **Fig. 1** Classification of cocoa butter alternatives.

Alternatives of Cocoa Butter

The cultivation of the *T. cacao* plant, the main source of cocoa butter, is limited to tropical areas due to its requirement of growing conditions such as climate and temperature. Other factors including natural disasters and infectious plant diseases may also affect the yield of cocoa beans. As time passed, the demand of cocoa butter increased due to rapid global economic growth. Eventually, a deficiency of cocoa butter happened, which resulted in a price increase for cocoa butter. Thus, CBAs have been explored in order to cover the increased demand for cocoa butter. There are various types of alternatives for cocoa butter that have been classified into different categories based on their fat composition. CBAs are classified into three types: CBSs, CBEs, and CBRs. According to Patel et al., non-lauric plant fats, known as CBEs, are comparable to cocoa butter in both physical and chemical aspects. CBEs can be mixed with cocoa butter in any quantity without affecting its characteristics. Conversely, CBRs are non-lauric fats having similar fatty acid distribution as that of cocoa butter. Unlike CBEs, CBRs are only slightly compatible with cocoa butter because their triglyceride structure is completely different. Lastly, CBSs are lauric plant fats that are chemically totally different than cocoa butter, although they resemble the physical similarities of cocoa butter. CBSs are only suitable to be used as a complete substitution for cocoa butter. [5]. In another words, CBRs can be used to replace cocoa butter. ▸ **Fig. 1**, adapted from Budianto and Kusmardini, shows the classifications of CBAs [21].

CBSs are another replacer of cocoa butter in the food industry. A limited quantity of CBSs can be implanted with cocoa butter without influencing the processing, and physiological and melting characteristics. CBSs do not necessarily have the same or similar physicochemical properties as cocoa butter. The degree of compatibility basically depends on the quality. CBSs contain high amounts of lauric and myristic acids. However, CBSs are chemically different from cocoa butter. So, CBSs are used as a whole replacement for cocoa butter [3]. Despite exhibiting an eutectic effect and chemical differences, CBSs do not require tempering, which is a step that is typically required in the final product of other CBAs [40–42]. Thus, CBSs can be used for products that require good stability since they do not require a tempering process like cocoa butter.

Due to similar physical and chemical characteristics, CBEs can be mixed with cocoa butter in any ratio without changing the end products' processing or melting and rheological characteristics. The end products will have similar characteristics as products utilizing cocoa butter as a raw material. Like cocoa butter, the main fatty acids found in CBEs include oleic acid, palmitic acid, and stearic acid. Most CBEs are made by combining various mixtures of palm oil, palm oil fractions, shea and illipe, sal and mango kernel fats, and other ingredients. Typically, CBEs are less expensive than cocoa butter. CBEs are further distinguished into two subgroups: cocoa butter extenders (CBEXs) and cocoa butter improvers (CBIs) [3, 22]. CBIs are similar to CBEs; however, CBEXs cannot be used in combination with cocoa butter in any amount. This is because CBIs have a high concentration of solid triglycerides. Thus, they are frequently employed to improve soft cocoa butter [3]. The hardness and melting resistance of chocolate are attributed to the types of CBAs used in the manufacturing process. Chocolate made from CBIs, which are SOS-rich fats, or CBEs that are highly solid at 36 °C, are sturdy and melt-resistant. According to Reddy and Prabhakar, chocolate and confectionery products produced from cocoa butter are inadequate for use in hot climates due to the high risk of melting. Therefore, lipids resistant to high temperatures must be used in these types of climates [42]. It has been suggested that adding SOS triacylglycerols or SOS-rich fats to cocoa butter or chocolate can improve the quality of chocolate, prevent fat bloom, make the butter harder, and shorten the tempering time. When cocoa butter fully melts, CBIs typically have higher temperature profiles than cocoa butter and continue to be solid [43].

Lastly, CBRs are another option provided to replace cocoa butter. Cisse and Yemiscioglu stated that CBRs do not contain lauric acid, so-called non-lauric fat [44, 45]. CBRs are synthesized from fractionated vegetable fats and have a high tolerance for cocoa butter. They are utilized to give final products glass retention and a sharp meltdown without tempering. CBRs are mostly used in compound coatings because of their specific compatibility with cocoa butter. It can be mixed with cocoa butter to produce compounds that work well for both moldings and coatings. Since the fats in CBRs are not from the lauric region, the resulting products will not taste soapy. The fact that compounds produced using CBR do not require tempering is crucial [46, 47]. As a consequence of the differences of their chemical properties, CBRs and cocoa butter can be combined in very small amounts without affecting the final product [44].

There are several additional benefits provided by CBAs. Lauric and hydrogenated fats are usually used to substitute cocoa butter. Blends of palm oil mid-fraction and stearic acid-rich tropical butter, known as CBEs, have high oleic and stearic acid contents without changing plasma blood cholesterol levels. Consequently, CBEs offer a viable and healthier substitute for cocoa butter. ▶ **Table 3** was adapted from Naik and Kumar and gives a summary in terms of the different properties of CBAs [3].

Applications of Cocoa Butter Substitutes in Various Delivery Systems

Chocolate-based drug delivery system

Research done by Biswas et al. studied and compared the physical, rheological, and sensorial properties and bloom formation of dark chocolate made with cocoa butter, CBSs and blends of both cocoa butter and CBSs. Characterization of chocolate made has been done, which includes bloom formation, rheological, textural behaviors, polymorphism, melting profiles, and particle size distribution (PSD). The overall characterization outcomes suggested that the physical and sensory features of chocolate with 5 g CBS/100 g blend were similar to those of cocoa butter chocolate. However, compared to cocoa butter chocolate, chocolate with 20 g CBS/100 g blend demonstrated noticeably inferior sensory qualities, especially flavor acceptance and hardness [48].

In addition, a study done by Karavasili et al. moved a big step toward research about the application of cocoa butter in oral dosage forms. This study worked on the incorporation of both hydrophilic and lipophilic drugs in chocolate-based dosage forms using cocoa butter as the raw material employing extrusion-based 3D printing. This study investigated the use of corn syrup and bitter chocolate for the preparation of the ink formulations to develop a pediatric-friendly oral dosage form [49].

Lipid-based drug delivery system

Cocoa butter has been used in the preparation for pharmaceutical and probiotics delivery applications. Research done by Satapathy et al. employed whey protein isolate (WPI) solution as the aqueous phase while cocoa butter was used as the fat phase in the formulation of emulgels. In this study, cocoa butter served as emulgel's structural agent. Milky white emulsions were formed when the WPI solution was added to the pale yellow-colored molten fat (cocoa butter). Previous research revealed that the amount of unsaturated fatty acids in fats may influence how the fats crystallize [50, 51]. In this case, fat crystals are not surface active. Hence, emulsifiers have been utilized to stabilize the fat-aqueous interface of the biphasic formulations. Moreover, the aqueous component of oil-in-water emulsions becomes more viscous when hydrocolloids are added, thus stabilizing the emulsion [51, 52]. WPI was suggested to be amphipathic naturally, which gives it surface active properties [51, 53]. Therefore, it is incorporated within the aqueous phase in this study. As an alternative to chocolate, the blend of cocoa butter and WPI-based emulgels can be considered for the delivery of probiotics and antimicrobial medications with longer shelf lives [51].

On the other hand, cocoa butter serves as a solid lipid in nano-delivery systems. Nano-delivery systems are classified into biopolymer, which consists of proteins and polysaccharides, and lipid-based systems. However, thermal and chemical processes cannot be controlled accurately in carbohydrates and protein networks [54, 55]. Instead, lipids were shown to be more encapsulation efficient and suitable for large-scale production [55, 56]. Ideally, a delivery system should be able to incorporate the encapsulated compounds into food matrices with good physicochemical stabil-

▶ **Table 3** Properties of subgroups of cocoa butter alternatives [3].

Properties	CBE	CBR	CBS
Types of fatty acids	Plant fats without lauric acid	Non-lauric acid fats	Fats containing lauric acid
Physical and chemical properties	Similar to cocoa butter in terms of its physical and chemical characteristics, such as melting point and polymorphisms	Similar to cocoa butter in terms of distribution, but its structure is triglycerides, which is completely different	Chemically different to cocoa butter, only similar to cocoa butter in terms of some physical similarities
Mixing properties	Able to be mixed with cocoa butter in any quantity without changing the characteristics of cocoa butter	Only able to be mixed with cocoa butter in small quantity	Only suitable to fully (100 %) substitute cocoa butter
Main fatty acid	Palmitic (P), stearic (S) oleic acid (O), Linoleic (L), arachidic acid (A)	Elaidic acid (E), stearic acid (S), palmitic (P), linoleic (L)	Lauric acid (L), myristic acid (M)
Main triglycerides	POP, POS, SOS	PEE, SEE	LLL, LLM, LMM
Examples	Sal fat, kokum butter, shea butter, palm oil, illipe butter	Oil rape seed oil, cotton seed oil, palm olein, hydrogenated oil, soya oil, ground nut oil	Palm kernel oil, MCT, cocoa oil

POP: 1,3 dipalmitin-2-monooleato glycerol, POS: 1-palmito, 2-olein, 3-sterin glycerol, SOS: 1,3 distearinmonooleate glycerol, PEE: Triglycerides with one palmitic acid (P) molecule and two erucic acid (E) molecules, SEE: Tryglycerides with one stearic acid (S) molecule and two erucic acid (E) molecules, LLL: Triglycerides with three linoleic acid (L) molecules, LLM: Triglycerides with two linoleic acid (L) molecules and one myristic acid (M) molecule, LMM: Triglycerides with one linoleic acid (L) molecule and two myristic acid (M) molecules

ity and maintain organoleptic qualities while using natural ingredients and solvent-free production techniques. It should maximize the uptake of encapsulated substances upon consumption and guarantee regulated release in reaction to a particular environmental stimulus. Lastly, it should be able to easily scale-up for industrial production [55, 57].

Formulation of oral dosage forms

The oral route of administration is always the most popular and preferred way for patients to take their medications. The usage of cocoa butter has been involved in the formulation of tablets recently. Cocoa butter has been used to produce FMTs in research done by Liew et al. due to its unique characteristics and properties. Cocoa butter FMTs provide several benefits compared to conventional tablets in terms of the manufacturing process. Expensive and huge machines such as tableting machines are not required for the production of cocoa butter FMTs. This manufacturing approach provides a lower capital expenditure commitment. This is because, unlike traditional orally disintegrating tablets (ODT) manufacturing techniques, cocoa butter FMT production just needs a freezer and a mold, both of which are readily available and reasonably priced for the majority of small- and medium-sized manufacturing facilities. In this study, the formulation with cocoa butter and 15 % corn starch showed acceptable results for characterization tests. The dissolution profile, one of the most important parameters, was comparable to the innovator product [58].

Moreover, cocoa butter was used as a taste masking agent for ibuprofen, which has a bitter taste. According to an article published by Obaidat et al., supercritical fluid technology was used to formulate tasteless cocoa butter microparticles containing ibuprofen. The drug's remarkable dispersibility within the polymer was revealed by physicochemical characterizations of the microparticle synthesized. The absence of a significant drug-polymer interaction was confirmed by DSC (Differential Scanning Calorimetry) and FTIR (Fourier Transform Infrared Spectroscopy) studies, with a few minor variations that might be attributed to physical interactions. The synthesized microparticles contain a good percentage of drug content, and the particle size analysis indicated that they could be easily formulated into various dosage forms. Medication release was enhanced after 30 min, which is appropriate for flavor masking formulas. Consequently, this developed approach was promising in masking ibuprofen's taste, which can further be formulated to a suitable pediatric dosage form [59].

Formulation of suppositories

Besides the oral dosage form, cocoa butter has also been studied for the preparation and formulation of suppositories. The development of suppositories dosage forms is not that advanced and fast-paced compared to the development of oral dosage forms. This might be due to the convenience provided by oral dosage forms, resulting in the slow-paced development of suppositories. According to Melnyk et al., the global suppository market is currently limited due to certain inconveniences for the patients, although suppositories have a very long history. This condition results in the insufficiency of the development of new drugs in this dosage form. However, suppository is the preferred option compared to oral dosage forms under certain conditions. For example, it's not suitable to give medications in tablet or suspension form to infants. It is generally acknowledged that the therapeutic effect of suppositories is due to the interaction of the medicinal substance and the base. To determine the stability of a connected-dispersed system, one of the most crucial factors is the base's ability to supply the required structural and mechanical qualities. The European Pharmacopoeia and the State Pharmacopoeia of Ukraine categorized the suppository bases used in the manufacturing of this dosage form as hydrophobic, hydrophilic, and diphilic [60]. While there are six main classes of suppository bases according to the USP, namely, cocoa butter, CBSs, glycerin gelatin, polyethylene glycol, surfactant basis and tablet suppositories or inserts [61].

In general, cocoa butter is made up of a mixture of triglycerides of saturated and unsaturated fatty acids. Thus, cocoa butter is hydrophobic and does not absorb a significant amount of water since it does not contain an emulsifier. Cocoa butter is a good alternative to produce a soft base when the necessary equipment is absent. This is because the base produced from cocoa butter is soft, does not irritate sensitive membrane tissue, and is easily accessible and convenient [60]. However, there is no ideal and perfect excipient. Cocoa butter has a few disadvantages that limit its uses as a suppository base. Cocoa butter is sensitive to temperature and has a relatively low melting point. Thus, cocoa butter and its suppositories must be stored either at a controlled room temperature or in the refrigerator. The temperature for storage should not exceed 25 °C to prevent melting. Polymorphism of cocoa butter does not provide benefits in the case of suppositories. This condition means that cocoa butter can very easily be overheated and, when it is, it may solidify as one of the lower melting polymorphs. This condition results in the production of unstable suppositories in which the suppositories are not set up properly and might melt or liquefy when handled by the end users. In addition, as with all fatty bases, cocoa butter suppositories may give a poor and erratic release of certain drugs. When drugs do not have a water-soluble form, like acetaminophen, cocoa butter should not be used as the base [61].

A study done by Chushenko et al. aimed to create cocoa butter bases for the preparation of suppositories with various active pharmaceutical ingredients using a casting method. The researchers concluded that the base produced in the study was well tolerated and did not have osmotic pressure. Cocoa butter in combination with lecithin, which is an emulsifier, has a lubricating moderate reparative action. The bases produced are recommended by the researchers for introduction of various types of medicinal substances such as thermolabile substances, volatile substances, enzymes and probiotics, substances with a high melting point, and dense and liquid extracts [62].

Future Trends of Cocoa Butter

Nowadays, the usage and applications of cocoa butter are not only limited to the food industry but have been expanded to the pharmaceutical industry. The market is driven by innovation and the introduction of new cocoa-based products as well as an increase in the use of cocoa in cosmetics and pharmaceuticals, which is raising the demand for chocolate [63]. Recently, cocoa butter has been further utilized in the pharmaceutical industry due to its unique characteristics, which include a melting point close to humans' body temperature. Cocoa butter acts as a lubricant, binder, delivery carrier, and release agent in the formulations of oral dosage forms and suppositories. The pharmaceutical industry never stops searching for novel functional excipients that offer functionalities beyond the excipients currently available. Cocoa butter is an excipient that has huge potential as a carrier for controlled release formulations or for enhancing bioavailability. This condition may lead to the exploration of cocoa butter's application in the pharmaceutical industry, especially lipid-based drug delivery systems.

In addition, as mentioned above, cocoa butter was applied as a solid lipid in a nano-delivery system. With the advancement of technology, nano-delivery systems will be further studied and developed in the future due to their advantages. Cocoa butter's lipid nature allows it to be incorporated in nano-delivery systems or lipid-based formulations. This condition may help to improve the solubility and absorption of hydrophobic drugs. Nowadays, the public feels miserable towards healthy lifestyles, organic foods, and ingredients. Thus, there is a growing consumer preference for natural and plant-based ingredients. The same condition goes for pharmaceutical products. Cocoa butter, which is extracted from the cocoa bean of *T. cacao* plant, meets the preferences of consumers.

In addition, research never ends in the pharmaceutical industry. Since cocoa butter consists of various bioactive compounds and displays potential health benefits such as antioxidants, more researchers will work together to study the potential therapeutic benefits of cocoa butter. For example, the usage of cocoa butter can be further studied in the areas of wound healing, dermatology, and inflammation management. The prospects of cocoa are bright and interesting. Ongoing research in the field of nutrition and health may result in the creation of cocoa-based products with increased health advantages, leveraging the natural antioxidant qualities and possible mood-enhancing effects of cocoa [63].

Conclusion

In summary, the uniqueness and properties of cocoa butter allow for the usage of cocoa butter to be further studied and expanded, especially in the pharmaceutical industry. The introduction of CBAs has overcome the obstacles faced in the production of cocoa butter, such as a limited yield from the production of cocoa butter's source, *T. cacao*. In the pharmaceutical industry, cocoa butter had been used in different types of drug delivery methods such as the nano-delivery system and the newly introduced chocolate-based drug delivery system. Except for the food industry, cocoa butter has been studied and applied extensively in other fields, which includes the cosmetics field, pharmaceutical industry, and others. Researchers and professionals from various fields are studying and working hard to amplify the benefits and uniqueness of cocoa butter when applied in the manufacturing of various types of products.

Contributors' Statement

Data collection: Y. H. Loke, H. C. Phang, N. Mohamad, P.E Kee; Design of the study: K. B. Liew; Analysis and interpretation of the data: Y. H. Loke, H. C. Phang, N. Mohamad, P.E Kee; Drafting the manuscript: Y. H. Loke, H. C. Phang, N. Mohamad, P.E Kee; Critical revision of the manuscript: Y. L. Chew, S.-K. Lee, C. F. Goh, C. I. Yeo, K. B. Liew

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Conflict of Interest

The authors declare that they have no conflict of interest.

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