ผลของกระบวนการผลิตและน้ำมันชนิดอื่นหรือน้ำกระสายยาต่อสมบัติเคมีกายภาพของน้ำมันมะพร้าว
Effect of Production Process and Addition of Other Oils/Vehicles on Physicochemical Properties of Coconut Oil

นิพนธ์ต้นฉบับ

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วารสารไทยเภสัชศาสตร์และวิทยาการสุขภาพ2564;16(1):63-71.

Original Article

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บทคัดย่อ

วัตถุประสงค์: น้ำมันมะพร้าวถูกใช้เป็นส่วนประกอบที่สำคัญในผลิตภัณฑ์เครื่องสำอางและเภสัชภัณฑ์หลายชนิด ถึงแม้ว่าน้ำมันมะพร้าวจะได้รับความสนใจอย่างมาก อย่างไรก็ตามการเกิดผลึกไขของน้ำมันนี้นับเป็นปัญหาที่สำคัญ การลดอุณหภูมิในการเกิดไขและจุดไหลของน้ำมันมะพร้าวอาจป้องกันการเกาะกลุ่มของไข งานวิจัยนี้ศึกษาผลของกระบวนการเตรียมน้ำมันมะพร้าวและผลของการเติมน้ำมันชนิดอื่นและน้ำกระสายยาต่อสมบัติเคมีกายภาพของน้ำมันมะพร้าว **วิธีการศึกษา:** น้ำมันมะพร้าวแบบต่าง ๆ ถูกเตรียมจากการบีบอัดเนื้อมะพร้าว (CO1) และส่วนใสจากการทิ้งให้ตกตะกอน (CO2) และนำส่วนใสที่ผ่านการกรองรอบที่ 1 (CO3) รอบที่ 2 (CO4) และ รอบที่ 3 (CO5) โดยน้ำมันมะพร้าวจากกระบวนการเตรียมดังกล่าวและน้ำมันมะพร้าวชนิด CO5 ที่เติมน้ำมันและน้ำกระสายยาชนิดอื่น ได้นำมาศึกษาสมบัติเคมีกายภาพด้านต่าง ๆ **ผลการศึกษา:** การทิ้งให้ตกตะกอนและผ่านการกรองช่วยลดอุณหภูมิการเกิดไขของน้ำมันมะพร้าวได้ โดยน้ำมันเปปเปอร์มินต์ เบนซิลเบนโซเอต และเอ็นเมทิลไพร์โรลิโดนได้นำมาใช้เป็นสารยับยั้งการเกิดไข ซึ่งการเติมสารทั้งสามนี้ช่วยลดอุณหภูมิการเกิดไขของน้ำมันมะพร้าว น้ำมันเปปเปอร์มินต์ และเบนซิลเบนโซเอตลดอุณหภูมิจุดที่เกิดการไหลของ CO5 ได้มากกว่าเอ็นเมทิลไพร์โรลิโดนอย่างมีนัยสำคัญ ที่ระดับความเชื่อมั่นร้อยละ 95 การเปลี่ยนแปลงลักษณะทางสัณฐานวิทยาของผลึกไขมีผลต่ออุณหภูมิจุดที่เกิดการไหลและอุณหภูมิการเกิดไขของ CO5 **สรุป:** น้ำมันเปปเปอร์มินต์ เบนซิลเบนโซเอตมีประสิทธิภาพในการลดอุณหภูมิจุดที่เกิดการไหลของ CO5 มากกว่าเอ็นเมทิลไพร์โรลิโดน

คำสำคัญ: น้ำมันมะพร้าว การผลิต สารเติมแต่ง สมบัติเคมีกายภาพ

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Abstract

Objective: Coconut oil (CO) has been used as an important component in various cosmetic and pharmaceutical products. CO is the most notably of interest; nevertheless, its wax crystallization is a major problem. The decrement of wax appearance temperature (WAT) and pour point (PP) of CO might prevent the wax agglomeration This research investigated the effect of production process and addition of other oils/vehicles on physicochemical properties of coconut oil. **Method:** Different COs were prepared. CO1 was prepared by pressing comminuted kernel mass, CO2 was prepared by subjecting CO1 to sedimentation and decanting, while CO3, CO4 and CO5 were prepared by filtering this supernatant once, twice and thrice, respectively. The physicochemical properties of COs were investigated together with CO5 through the addition of additives such as oils and vehicles. **Results:** Sedimentation followed by filtration lowered the wax appearance temperature (WAT) of COs. Peppermint oil (PO), benzyl benzoate (BB) and *N*-methyl pyrrolidone (NMP) were chosen as wax inhibitors. Lower WAT values were achieved owing to the addition of PO, BB and NMP. Here PO and BB significantly more decreased the pour point (PP) of CO5 than NMP ($p < 0.05$). Changes in wax crystal morphology influenced PP and WAT of CO5. **Conclusion:** PO and BB were more effective in decreasing WAT of CO5 than NMP.

Keywords: coconut oil, production, additives, physicochemical properties

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Introduction

To design the controlled release intramuscular injectable preparations, vegetable oils have been of interest as oily vehicles.[1] According to the USP specification, the oil for an injectable vehicle must origin from vegetables and should be liquid at room temperature.[2,3] The most commonly used oils are castor oil, corn oil, cottonseed oil, olive oil, peanut oil, sesame oil, soybean oil, hydrogenated vegetable oil and medium - chain triglyceride of COs and palm oil.[4]

Coconut oil (CO) contains free fatty acids, triacylglycerols, partial glycerides, phospholipids, sterols and tocopherols.[5] It has been used as an important component in shampoo, soap, toothpaste, cleaning agent and foaming booster.[6,7] Moreover, it has been used as a lotion for the eradication of head lice.[8] CO has been used as the component for self-nanoemulsifying drug delivery system[9], microemulsion of haircare product[10] and oil pulling.[11] CO contains more than 90% saturated fatty acids, has a low iodine value[12-15] and tends to be solid with wax formation occurring at room temperature.[6,7] Thus, CO in the form of fractionated coconut oil has been used as an oily vehicle in injectable preparations or components of micro/nanoparticles for drugs that are unstable or insoluble in aqueous media. However, many steps are required to reduce saturated fatty acid in COs, and they include hydrolysis, distillation and re-esterification; these processes make it expensive and cause a loss of beneficial substances.[8] Although CO is the most notably of interest as a vehicle for injectable preparations, wax crystallization is a major problem associated with CO which tends to be solid at room temperature.[7] Normally, to reduce the wax crystallization of oil, wax inhibitors, flow improvers or wax crystal modifiers are incorporated.[12] The present study aims to investigate the effect of various oils and pharmaceutical vehicles as wax inhibitors of COs. We investigated the decrement of wax appearance temperature (WAT) and pour point (PP) and modified the wax crystal behavior of CO in order to prevent wax agglomeration and deposition. The WAT could be determined from the cloud point (CP) which is the temperature that the first wax crystals occur in a liquid. It depends on the concentration and molecular weight of waxes and the chemical nature of non-waxy parts in the oil.[13] Moreover, USP specification states that the oil used as vehicles should be liquid at room temperature and should have a WAT not higher than 15 °C.[3] The present study investigated the effect of oil production steps and additives including other oils and pharmaceutical vehicles on the physicochemical properties of CO.

Methods

Materials

Olive oil (OO) (lot no. L9126R H1336, Sino-Pacific Trading Co., Ltd., Bangkok, Thailand), PO (P. C. Drug Center Co., Ltd., Bangkok, Thailand), sunflower oil (SO) (Sino-Pacific Trading Co., Ltd., Bangkok, Thailand), sesame oil (SO) (Namsiang Co., Ltd., Bangkok, Thailand) and light mineral oil (MO) (P. C. Drug Center Co., Ltd., Bangkok, Thailand) were used as additive oils. Benzyl alcohol (BA) (batch no. OD05AF1, P. C. Drug Center Co., Ltd., Bangkok, Thailand), benzyl benzoate (BB) (Pharmaceutical Traders Co., Ltd., Bangkok, Thailand), isopropyl myristate (IM) (Ake-Trong Chemical 1985 Co., Ltd., Bangkok, Thailand), ethyl oleate (EO) (lot no. 1425705, Sigma-Aldrich Chemie GmbH, Buch, UK) and *N*-methyl-2-pyrrolidone (NMP) (lot no. A0277037, ACROS, New Jersey, USA) were used as mixed vehicles in this study.

Preparation of modified COs

Coconut meat collected from ripe coconut nut from Surat Thani province, Thailand was grated to comminuted kernel. After drying in a tunnel hot- air dryer (55 – 65 °C), the comminuted kernel mass was passed through a screw press to expel the oil (CO1). Then it was allowed to sediment in a plastic container for 30 days at room temperature, after which the supernatant (CO2) was decanted from the sediment. The supernatant was filtered in 3 steps at room temperature, starting with a 10-micron filter (CO3), 5-micron filter (CO4) and 3-micron filter (CO5). Then, the most suitable CO was chosen after determining the COs PP, wax appearance under microscope, degradation temperature (thermogravimetric analysis, TGA), the lowest temperature at which the oil viscosity can still be detected (LVD), melting point (MP) and the WAT. Additives were added to the selected CO so that the additive-to-CO ratio by weight was 1:1. The additives used were oils and vehicles. SO, OO, SFO, PO and MO were used. The vehicles were EO, IM, BB, BA and NMP. Then the WAT was determined using ASTM standard method,[14] LVD and viscometry method. The other physicochemical properties of selected modified COs were evaluated using differential scanning calorimetry (DSC) and microscopy analysis.

Evaluations

Pour point (PP) measurement

The PP, that is, the lowest temperature at which the oil still pours when cooled was determined by the ASTM D97 method.[14] After heating five COs to 45 °C, they were allowed to cool to facilitate wax crystal formation. Every 3 °C decrement, the container was checked for oil movement by tilting until the sample stopped moving. The point at which the oils stopped moving when held in a horizontal position for 5 s was determined to be above 3 °C, and this was recorded as the PP (n = 3).

Determination of wax crystal by microscopy

The wax crystal behavior of COs was investigated using a hot stage microscope (HSM) (Mettler Toledo FP900 Thermosystem, Mettler Toledo AG, Switzerland). The COs were dropped onto a glass slide and covered with a glass coverslip. The glass slide was then inserted into the stainless stage, which has a hole at the center through which light from the microscope can pass through. The temperature of the stainless stage was gradually cooled with circulating cooling water bath from 30 °C to 5 °C with a 1 °C/min decreasing rate. The image of wax crystals was taken at 5 °C using a digital camera coupled with the eyepiece of the microscope at 100 x magnification.

Study of thermal degradation behavior by TGA

The thermal degradation behavior of COs prepared from different processes was studied using a thermogravimetric analyser (PerkinElmer Pyris, USA). Approximately 10 mg of the oils were weighed into an open alumina crucible. The dynamic experiment was carried out at a heating rate of 10 °C/min in temperature ranging from 30 °C to 550 °C in air atmosphere. Thermogravimetric (TG) curve and derivative thermogravimetric (DTG) curve were used in this study.

WAT determination

The formation of visible wax crystals depends on the concentration and molecular weight of the waxes and the chemical nature of the non-waxy parts in the oil. The temperature at which the visible wax crystals occurred (i.e. WAT) was determined using viscometry, ASTM standard and DSC.[10,16]

Viscometry method

The viscosities of the COs prepared from different processes were measured using a Brookfield viscometer (Brookfield Engineering Laboratories, Inc., USA) with cone spindle CPE-40. The viscosity was studied in the temperature ranging from 40 °C to 0 °C at 25 s^{-1} shear rates and recorded at every decrease of 2 °C (n = 3). The lowest viscosity detectable temperature is the lowest temperature at which the equipment can read the viscosity. The WAT of the oils was determined from the plots of viscosity versus temperature. The WAT was detected at the point at which the curve diverged.

ASTM standard method

The ASTM standard method is the most routinely used method to determine WAT. In this method, the temperature at which a CP of wax crystals first appears in a liquid, i.e. the temperature at which wax precipitation begins, is investigated; here, the CP is determined by the ASTM D2500-17a method.[15] First, COs prepared by different processes were heated to 45 °C in a water bath to dissolve the precipitated wax, and they were then allowed to cool for wax crystals formation. At every 1 °C decrement, the container was checked for the formation of cloud wax crystals. The temperature at which cloudiness was observed at the bottom of the test jar was recorded as the CP (n = 3).

DSC method

DSC thermograms of COs obtained from different processes were investigated using a differential scanning calorimeter (Model DSC7, Perkin Elmer, USA) operated under nitrogen gas atmosphere. The oils of 10 mg were weighed accurately into an open aluminium pan and placed in a differential scanning calorimeter module with a similar empty pan as reference. Both cooling and heating experiments were determined. In the cooling experiment, the oils were heated to 50 °C (heating rate of 10 °C/min) to dissolve any precipitated wax in the oil. Then, the oils were cooled to -50 °C at a steady cooling rate of 5 °C/min using a liquid nitrogen. In the heating experiment, after the oils were cooled to -50 °C, they were heated to 50 °C at a steady rate of 5 °C/min.

Statistic data analysis

The experimental measurements were carried out in triplicate and the values were expressed as mean ± SD. The statistical significance of viscosity, PP and CP were examined using one-way analysis of variance. The significance level was set at P-value < 0.05. The analysis was performed using SPSS for windows.

Results and Discussions

Physicochemical properties of Cos

Pour point (PP) of COs

The PP values of the proposed COs were in the range of 18 - 20 °C (Table 1A). No significant difference existed between the PP values, proving that the process of sedimentation followed by filtration used in COs production did not affect the PP value.

Crystal behavior of COs by HSM analysis

The difference in wax crystal behavior between the COs is shown in Figure 1. As shown, CO1 and CO2 exhibited stellate-shape crystal, while CO3, CO4 and CO5 exhibited spherical crystals surrounded by small needle-like spikes. This corresponds with a previous report in which the crystal morphology of CO was a spherulite consisting of needle-like crystals.[16-19] However, the filtration process contributed to a change in the COs crystal morphology. The undissolved wax usually removed from CO by filtration and sedimentation promotes the more transparent CO in which its wax crystal was also changed after cooling.

Table 1 Physicochemical properties of COs prepared from different processes (A); LVD and WAT of the mixing systems between oils and CO5 (n = 3) (B); LVD and WAT of the mixing systems between vehicles and CO5 (n = 3) (C) and physicochemical properties of other oil/vehicle and CO5 (D).

(A)

Sample	PP ± SD (n = 3) (ºC)	WAT ± SD (°C) Viscometry (n = 3)	ASTM (n = 3)	DSC	LVD ± SD (n = 3) (°C)	MP (°C)
CO1	19.0 ± 1.7^{a}	24.7 ± 0.6^{a}	25.7 ± 1.2^{a}	10.0	12.0 ± 0.0^{a}	26.3
CO2	18.0 ± 0.0^{a}	22.7 ± 1.2^{b}	23.7 ± 0.6^{b}	8.0	10.7 ± 1.2^{b}	26.4
CO3	20.0 ± 1.7^{a}	22.7 ± 2.3^{b}	23.3 ± 0.6^{b}	7.9	10.0 ± 2.0^{b}	26.4
CO4	19.0 ± 1.7^{a}	21.3 ± 2.3^{b}	23.3 ± 0.6^{b}	8.7	10.7 ± 1.2^{b}	26.5
CO5	19.0 ± 1.7^{a}	21.3 ± 2.3^{b}	23.3 ± 0.6^{b}	8.0	10.0 ± 2.0^{b}	26.4

(B)

Sample	CO+PO	CO+MO	CO+SO	CO+SFO	CO+OO	CO
LVD±SD (°C)	2.0 ± 0.0	4.7 ± 1.2	4.7 ± 1.2	13.3 ± 1.2	4.7 ± 1.2	10.0 ± 2.0
WAT±SD (°C)	15.3 ± 1.2^{a}	21.3 ± 1.2^{b}	19.3 ± 1.2^{b}	32.7 ± 1.2^{c}	23.3 ± 1.2^{b}	21.3 ± 2.3^{b}

(C)

Sample	CO + BB	CO + NMP	CO + BA	CO + EO	CO + IM	CO
LVD±SD (°C)	2.7 ± 0.6	4.7 ± 1.2	3.0 ± 1.0	4.7 ± 1.2	3.0 ± 1.0	10.0 ± 2.0
WAT±SD (°C)	11.3 ± 1.2^{a}	12.7 ± 1.2^{a}	13.3 ± 1.2^{a}	16.7 ± 1.2^{b}	12.7 ± 1.2^{a}	21.3 ± 2.3^{c}

(D)

Sample	PP ± SD (n = 3) (°C)	LVD ± SD (n = 3) (°C)	MP (°C)	WAT ± SD (ºC) Viscometry (n = 3)	ASTM (n = 3)	DSC
CO	19.0 ± 1.7^{a}	10.0 ± 2.0^{a}	26.4	21.3 ± 2.3^{a}	23.3 ± 0.6^{a}	8.0
CO + PO	3.0 ± 0.0^{b}	2.0 ± 0.0^{b}	17.6	15.3 ± 1.2^{b}	11.0 ± 2.0^{b}	-8.9
CO + BB	3.0 ± 0.0^{b}	2.7 ± 0.6^{b}	16.7	11.3 ± 1.2^{c}	10.7 ± 0.6^{b}	-8.8
CO + NMP	6.0 ± 0.0^{c}	4.7 ± 1.2^{c}	18.5	12.7 ± 1.2^{c}	15.0 ± 0.0^{c}	-4.1

Note: The superscript alphabet represents a statistical significance (*P*-value < 0.05) of the data which the same alphabet means "not different by statistical significance" whereas the different alphabet means "different by statistical significance."

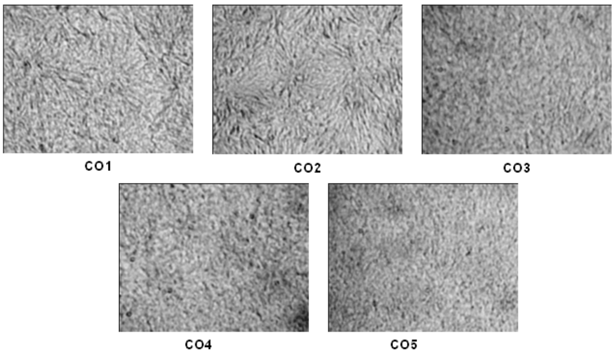
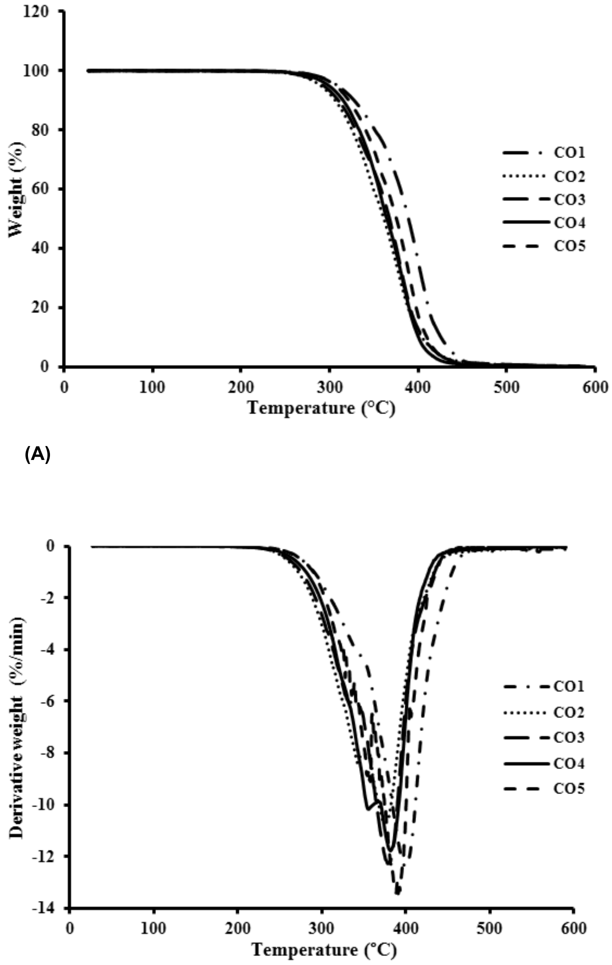


Figure 1 Photographs from HSM analysis of COs prepared from different processes (x100).

Thermal degradation behavior by TGA

Figures 2A and 2B depict the TG and DTG curves of COs respectively. The TG curves almost superimpose with each other, except that of CO1, which shows a shift in response to a higher temperature. The COs decomposed in the temperature range of 250 – 450 °C. The DTG curves of CO4 and CO5 exhibit two degradation stages. The temperatures for the maximum degradation rate (T_{max}) of CO4 were 356 °C and 381 °C with weight losses of 40% and 70%, respectively. The T_{max} values of CO5 were 356 °C and 391 °C with corresponding weight loss values of 33% and 71%, respectively. The DTG curve of CO1, CO2 and CO3 exhibits a single stage of degradation with T_{max} values of 400 °C, 376 °C and 379 °C and the weight losses of 64%, 66% and 65%, respectively. This result indicates that CO1 was more thermally stable than CO2 - CO5 because it had the highest T_{max}.



(A)

(B)

Figure 2 TG (A) and DTG (B) curves of COs prepared from different processes.

Wax appearance temperature (WAT)

From WAT determinations, viscometry method, ASTM standard method and DSC technique were applied for this research since these methods were suitable and applicable in field of pharmaceuticals and the related instruments were accessible. The viscosities of COs decreased with an increase in the temperature; however, there was no significant difference between the viscosities (Figure 3). The LVD is the temperature at which oil changes into semisolid; thus, at this temperature, the viscosities of the oil are extremely increased. However, the equipment could still detect the temperatures. The LVD of CO1, CO2, CO3, CO4 and CO5 were 12.0 ± 0.0, 10.7 ± 1.2, 10.0 ± 2.0, 10.7 ± 1.2 and 10.0 ± 2.0 °C, respectively. The data show no significant difference between the LVDs of the COs. It is evident that the sedimentation followed by filtration process did not affect viscosity and the LVD. The 90% saturated fatty acids still remains dissolving in such COs[16,17]; thus, their viscosity and LVD were not significantly changed. The limitation of CO for the use as an injectable vehicle was the wax formation at room temperature. Therefore, the decreased WAT can possibly diminish this problematic behavior. The WAT, also known as CP, is the temperature at which the first wax crystals occur in a liquid. It depends on the wax concentration, molecular weight and the chemical nature of the non-waxy component in the oil.[13] The WATs of COs from viscosity measurements are shown in Figure 3 and Table 1. The WATs of CO2, CO3, CO4 and CO5 are not significantly different but are significantly different from that of CO1 (*P*-value < 0.05) (Table 1). From the viscosity measurements, the resistance of fluid to flow can be determined to indicate a wax deposition. Heat promotes the kinetic motion and breakage of intermolecular bonds between adjacent layers and consequently decreases a viscosity of oil.[18,19] On the other hand, a lower temperature makes the oil more viscous, and a sufficient decrease in temperature results in wax precipitation in the oil.

The DSC thermograms of different COs from cooling and heating experiments are shown in Figure 4. In the heating experiment, a broad endothermic peak of COs was observed at approximately 24 °C, whereas two exothermic peaks were observed for CO1 and CO5 in the cooling phase, and they occurred between 5 °C and 6 °C and between -22 °C and -23 °C, respectively. Moveover, CO2, CO3 and CO4 showed three exothermic peaks in which two peaks were seen between 1 °C and 5 °C and the other between -10 °C and -22 °C. The DSC thermograms can also determine not only the MP but also the WAT of a sample.[20,21] MP of COs was detected at a temperature in the range of 26.3 °C - 26.5 °C. A previous study has also found the MP of CO to be between 20 °C - 28 °C.[22]

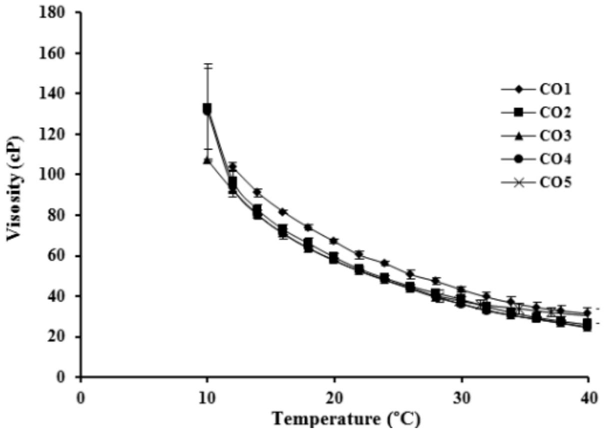
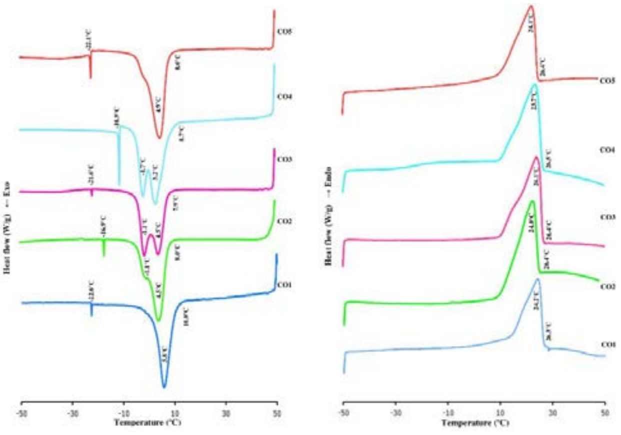


Figure 3 Viscosity temperature profiles of COs prepared from different processes (n = 3).

To detect the WAT of COs, only the cooling curve was selected. The onset temperature was assessed as the tangent point, where the heat flow that began to decrease was reported as the WAT.[21] The WATs of CO2 - CO5 were found to be approximately 8 °C, while that of CO1 was about 10 °C. The finding indicates that the WAT of COs investigated by DSC was lower than those determined by ASTM standard and viscometry methods (Table 1). According to the WAT determination by viscometry, the ASTM standard method and DSC method, the WATs of CO2, CO3, CO4 and CO5 were not statistically different; however, they were statistically different from that of CO1, indicating that the sedimentation followed by filtration process efficiently lowered the WAT of COs. Typically, the filtration aims to separate the undissolved wax and the sedimentation promotes the precipitation of the protein from CO. The supernatant was filtered starting with a 10-micron filter (CO3), 5-micron filter (CO4) and 3-micron filter (CO5), respectively, to minimize an energy consumption and effectiveness of filtration. The more transparent CO was obtained after passing these processes. The manufacturer selected CO5 as the commercial product, although the filtration process slight altered the WAT. The addition of other oils and vehicles were employed further for modifying the WAT of CO5.



(A) (B)

Figure 4 DSC thermograms of COs prepared from different processes in cooling (A) and heating (B) experiments.

Effect of other oils and pharmaceutical vehicles

Oil CO5 is the industrial finished product, which can be employed as commercial oil. Thus, CO5 was selected as a representative oil for the further study of wax inhibition in COs upon the addition of additives, and it is abbreviated as CO. Viscosity measurements were carried out. The proper modified CO with additive was chosen. The WAT was set not higher than 15 °C according to the ASTM standard method. This was because the USP specifies that the oil used as vehicle should be liquid at room temperature.[3] Physicochemical properties of selected modified COs were evaluated.

Meanwhile, it was observed that SFO addition led to an increase in the LVD of CO (13.3 ± 1.2 °C) and SO, OO and MO decreased the corresponding LVDs of CO to 4.7 ± 1.2 °C (Fig. 5, Table 1B). There is no significant difference between the obtained LVDs. However, the LVD upon the addition of PO to CO gave the lowest (2.0 ± 0.0 °C). The LVD was apparently lowered when vehicles were added. However, the LVDs for systems mixed with IM (3.0 ± 1.0 °C), BB (2.7 ± 0.6 °C), and BA (3.0 ± 1.0 °C) were lower than those of the systems mixed with EO and NMP (4.7 ± 1.2 °C), but no significant difference existed between the LVDs. According to the results, the addition of PO decreased the viscosity, LVD and WAT of CO. A previous study also used PO as an excipient for doxycycline hyclate-loaded eudragit RS *in situ* forming gel using NMP as a solvent for periodontitis treatment.[23] Therefore, PO was chosen as the representative oils to incorporate with CO.

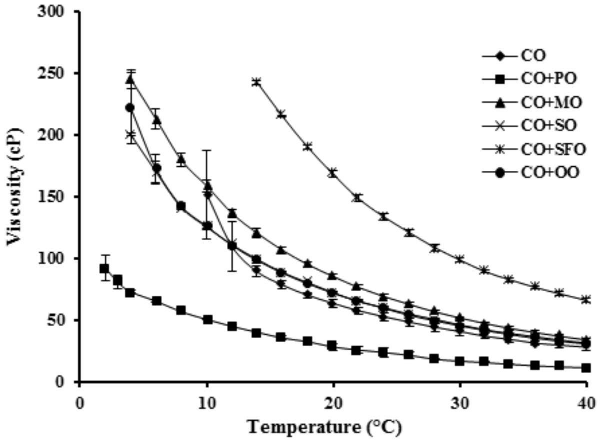


Figure 5 Viscosity temperature profiles for the mixing systems between oils and CO (n = 3).

Although the viscosity, LVD and WAT were decreased for all vehicles, as shown in Table 1C and Figure 6, NMP was selected because it is a water-soluble organic solvent. It is usually combined with a non-aqueous solution in injectable formulations[4,24] and has also been used as a solvent for the injection preparation of Eligard®.[4] Being a solubilizing agent and a non-aqueous solvent in intramuscular injections[25], BB was also selected as an additive. It is also used as a co-solvent in oily injection solutions of Dimercaprol® and in the preparation of hormone such as androstenediol dipropionate, testosterone propionate, hydroxyprogesterone carbonate and cyproterone acetate.[26,27]

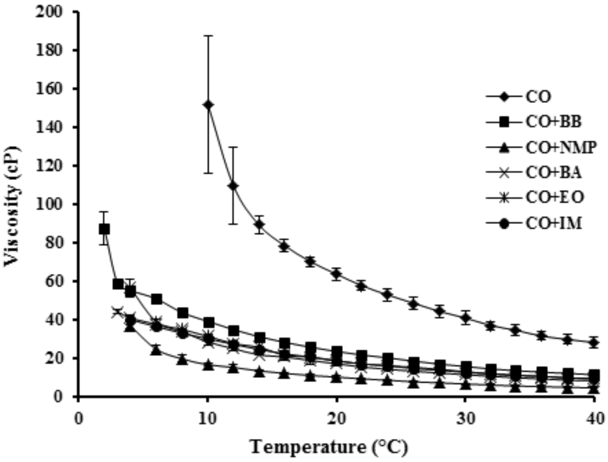
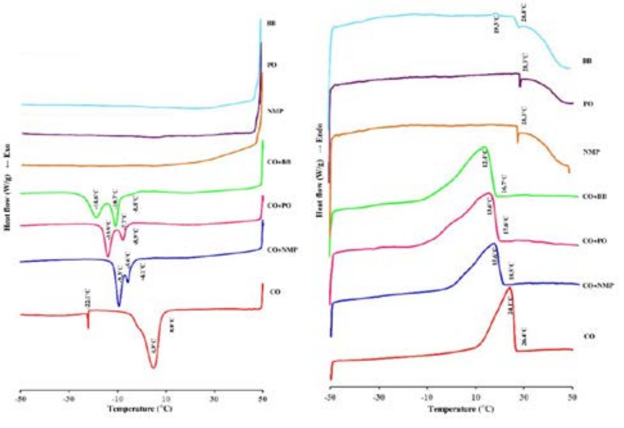


Figure 6 Viscosity temperature profiles for the mixing systems between vehicles and CO (n = 3).

Physicochemical properties

Finally, the selected modified COs (CO+PO, CO+BB and CO+ NMP) were investigated for their physicochemical properties and the results are presented in Table 1D. The addition of PO and BB significantly decreased the PP of CO more than NMP (P-value < 0.05). The DSC thermograms in the cooling experiment showed no melting peak of NMP, BB and PO. However, two exothermic peaks were observed in CO and the selected modified COs (Figure 7A). The peaks of CO+BB were found at a lower temperature than those of CO+PO and CO+NMP. The WAT of CO was obtained from the onset of crystallization. The WAT of CO was higher than those of CO+NMP, CO+BB and CO+PO (Figure 7A). In the heating DSC experiment, PO and NMP exhibited an exothermic peak at 28.3 °C, but BB exhibited an exothermic peak at 28.8 °C and an endothermic peak at 19.3 °C (Figure 7B). The endothermic peak in the heating experiment of selected modified COs occurred at a lower temperature than that of CO. Among the selected modified COs, the endothermic peak of CO+BB occurred at lower temperature than that of CO+PO and CO+NMP. In addition, the lowest MP was observed in CO+BB, followed by CO+PO and CO+NMP. Meanwhile, CO exhibited the highest MP. Thus, the additions of PO and BB to CO were more effective in decreasing the WAT and MPs than the addition of NMP. Similarly, the WAT of CO from ASTM standard method was lower when PO, BB and NMP were employed. The WAT of CO from ASTM decreased upon BB and PO addition markedly greater than that upon NMP addition ($p < 0.05$). The WAT from viscometry method indicated that the WATs of CO+BB (11.3 ± 1.2 °C) and CO+NMP (12.7 ± 1.2 °C) were lower than those of CO+PO (15.3 ± 1.2 °C) and CO (21.3 ± 2.3 °C). This efficient lowering WAT of CO should result from the wax solubilizing effect of PO, BB and NMP because they could promote the dissolution of the main saturated fatty acids of CO owing to their hydrophobicity and solubilizing property.[23-25]

By comparison, PO, BB and NMP diminished the viscosity, LVD and WAT of CO in which the addition of PO and BB significantly minimized the PP of CO more effectively than the addition of NMP (P-value < 0.05). CO+BB presented the lowest melting temperature (16.7 °C). Apparently, PO and BB were more effective in lowering the WAT and melting temperature of CO than NMP. This superiority of modified COs is expected for their utilizations as vehicle of injectable dosage forms; nevertheless, their compatibility, stability and safety characteristics should be further conducted.



(A) (B)

Figure 7 DSC thermograms of selected modified COs in cooling (A) and heating (B) experiments.

The wax crystal morphologies of selected modified COs were investigated under HSM as shown in Figure 8. Large crystals were observed in CO+PO at 5 °C, while stellate-shaped crystals were found in CO+BB at 5 °C. The CO+NMP exhibited a round shape with small - sized crystals at 5 °C. These changes in crystal size could prevent wax formation.[28] The addition of a PP depressant could change the crystal size of palm oil methyl esters and effectively reduce the PP and CP of this substance.[29] These changes in crystal morphology influenced the PP, LVD and WAT of CO. Therefore, the observation of wax crystal morphology should be conducted for understanding the microstructure change of processed CO.

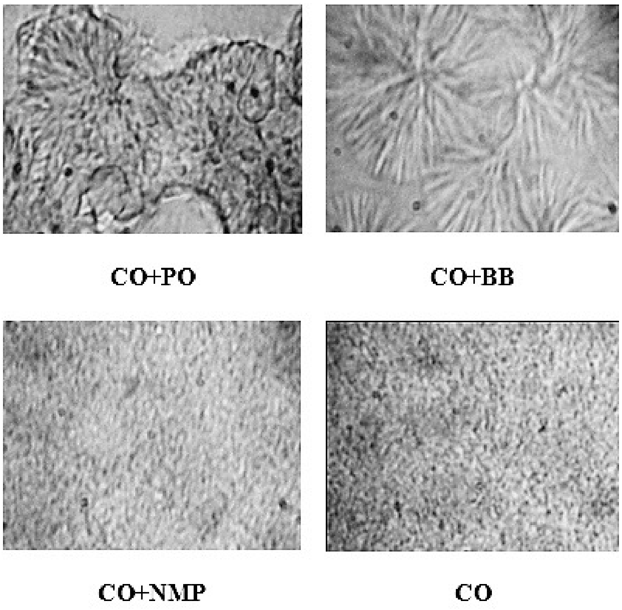


Figure 8 Photographs from HSM analysis of selected modified COs at 5 °C (X100).

Conclusion

In the present study, oil CO1 was obtained by pressing comminuted kernel mass. CO2 was the supernatant that emerged from CO1 after 30 days of sedimentation. Then, CO3 was obtained through filtration of this CO2 supernatant with 10-micron filter, while CO4 was obtained by filtration of CO3 supernatant through a 5-micron filter, and CO5 was obtained by filtration of CO4 supernatant with a 3-micron filter. The method of sedimentation followed by filtration induced the change in the crystal morphology and lowered the WAT of COs but did not affect the viscosity and LVD of the COs. Thermal degradation behavior determined by TGA analysis indicated that CO1 was more thermally stable than CO2 - CO5. The effect of additives was determined by the physicochemical properties of the industrial finished product, CO5. All vehicles including PO, BB and NMP decreased the viscosity, LVD and WAT. The addition of PO and BB significantly decreased the PP of CO more than the addition of NMP (P-value < 0.05). In comparison, CO+BB presented the lowest melting temperature (16.7 °C). Thus, PO and BB were more effective in decreasing the WAT and melting temperature of CO than NMP. Nevertheless, the compatibility and safety of these modified COs as the component in the injectable dosage forms should be further investigated. By comparison, the WAT value from determination of CP using ASTM standard method was interesting. It provided the reliable information since this method measures the temperature at which cloudiness of oil was observed at the bottom of the test jar. Thus, the wax formation with cloudiness observation could be directly determined. The rather difficulty was obtained for checking a point at the curve diverged from the viscometry method whereas the wax from DSC technique had to use the complicate instrument with rather high expenditure.

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