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Onoceranoid Triterpenes of *Lansium domesticum* Corr. cv. Kokossan and Their Cytotoxicity against MCF-7 Breast Cancer Cells

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Abstract

The onoceranoid triterpenes isolated from the kokossan fruit peels were studied *in vitro* using MCF-7 breast cancer cells. Three onoceranoids, namely 8,14-secogammacera-8(26),14-dien-3,21-diol (**1**), 3*β*-hydroxyonocera-8(26),14-dien-21-one (**2**) and α,γ-onoceradienedione (**3**), were obtained from the ethyl acetate extract of kokossan fruit peels. Compounds **1** - **3** were obtained for the first time from this cultivar. Several spectroscopic methods, including IR, HR-TOFMS and 1,2 D-NMR, were used to determine the chemical structures of compounds (**1** - **3**), and the results were compared to spectrum data that had previously been published. Additionally, the activity of compounds **1** - **3** was assessed *in vitro* using MCF-7 cells. With an IC_{50} value of 17.11 µg/mL, compound **2** demonstrated the highest activity in the activity test findings, followed by compounds **3** and **1**, with IC_{50} values of 19.66 and > 150 µg/mL, respectively. When compared to cisplatin as a positive control, compounds **2** and **3** showed considerable potency, while compound **1** showed no activity. Compounds **2** and **3** were the most promising candidates for the anticancer drug; nevertheless, more testing is necessary to ascertain their biological mechanism for future research.

Keywords: *Lansium domesticum* Corr. cv. Kokossan, MCF-7 breast cancer cell, Onoceranoids

Introduction

The Meliaceae family includes the tropical fruit-bearing plant *Lansium domesticum*, which is valued for its traditional medicinal uses as well as for its economic worth [1,2]. Many of the species in the Meliaceae family, commonly known as the mahogany family, are important from an ecological and medicinal standpoints [3,4]. The many medical effects of members of this family, such as *L. domesticum*, are attributed to their abundance of bioactive chemicals, including terpenoids (steroids, sesquiterpenoids, tetranortriterpenoids and triterpenoids) [5-10], steroids [11,12] and alkaloids [13]. *L. domesticum* is well known to have therapeutic potential because traditional medicine has used it for antidiarrheal, antimalarial, antioxidant, anti-inflammatory, antibacterial and antifeedant properties [14,15]. These pharmacological actions are largely attributed to the plant's bioactive constituents, especially terpenoids and steroids, with onoceranoid-type terpenoids making up approximately 37.5 % of the chemical composition in this species. This

highlights the chemical diversity within the Meliaceae family and its potential for therapeutic applications [1,2,7,16,17].

L. domesticum is a tropical plant that is often found in Thailand, Australia and Indonesia Despite this, research on *L. domesticum*, particularly its diverse chemical profiles, remains underdeveloped. While past studies have largely focused on the plant's medicinal potential, especially in traditional applications, there is a lack of in-depth chemical characterization of specific cultivars of *L. domesticum*. In Indonesia, the 3 primary cultivars, duku, kokosan and langsat, each exhibit distinct chemical compositions [20]. Previous research on the *L. domesticum* cv. Kokossan cultivar has specifically concentrated on the stem bark's terpenoid-rich *n*-hexane extract, which demonstrated modest cytotoxic action against MCF-7 breast cancer cells (IC_{50} = 42.95 µg/mL). Moderate activity was also exhibited by the sesquiterpenoid eudesm-4(15),7-dien-1β-ol that was obtained from this extract [5,21]. These findings underscore the potential of Meliaceae species like *L. domesticum* as sources of bioactive compounds with medicinal value.

Despite the promising bioactivity observed in *L. domesticum*, particularly the kokossan cultivar, the chemical constituents of this variety remain underexplored. This study aimed to address this gap by focusing on the isolation and structural elucidation of compounds **1** - **3** from *L. domesticum* Corr. cv. kokosan. Unlike previous studies, which primarily focused on general pharmacological evaluations, this research provided a detailed chemical characterization of this underexplored cultivar. Notably, compounds **1** and **2** were produced by the reduction of α,γ-onoceradienedione (**3**), marking the first time these compounds have been isolated from this genus [22] through reduction of α,γ-onoceradienedione (**3**). In addition, the study evaluated the cytotoxic activity of these compounds against the MCF-7 cancer cell line, contributing valuable insights into the therapeutic potential of the *L. domesticum* kokosan cultivar. By doing so, this research not only added to the growing body of knowledge on the Meliaceae family but also highlighted the untapped chemical diversity within *L. domesticum*, providing a foundation for the development of novel therapeutic agents.

Experimental section

Tools and materials

The extract and fractions were concentrated using a Buchi R-144 rotary evaporator equipped with a Buchi B1669 vacuum system. Compound separation was carried out using both column chromatography and thin-layer chromatography (TLC), with detection achieved using a UV detector lamp at wavelengths of 254 and 365 nm. The analysis and characterization of the pure isolates were performed with an 8425A Diode Array UV spectrophotometer. Infrared (IR) absorption was measured using a Shimadzu FTIR 8400 instrument with a KBr plate, while nuclear magnetic resonance (NMR) spectra were recorded on a JEOL ECZ 500R spectrophotometer operating at 500 MHz for ^{1}H-NMR and 125 MHz for ^{13}C-NMR. Molecular mass determination was conducted using a Qtof MS ESI Acquity UPLC System mass spectrophotometer. Silica gel 60 was employed as the stationary phase for column chromatography, and TLC plates were precoated with GF254 silica gel (Merck, 0.25 mm). Detection during chromatography was enhanced by spraying with a 10 % H_2SO_4 in ethanol solution, followed by heating. Cytotoxic activity was tested using a 96-well plate, an incubator and a microplate reader.

Isolation of compounds from *L. domesticum* Corr. cv. *Kokossan* fruit peels

The fruit peel of *L. domesticum* Corr. cv. Kokossan as much as 1.7 kg was cleaned, dried and pulverized. The fruit peel was then macerated for 3 separate 24-hour periods at room temperature with *n*-hexane, ethyl acetate and butanol. After that, the macerates were evaporated in a rotary evaporator set to low pressure and 40 °C until three extracts, *n*-hexane, ethyl acetate and methanol, were produced. Using *n*-hexane as the mobile phase or eluent (gradient 10 % 100:0 - 0:100) and a polar stationary phase, specifically silica G60 F254 (230 - 400 mesh), the concentrated ethyl acetate extract (60 g) was separated by vacuum liquid chromatography (VLC), resulting in five fractions (A - E).

Fraction D (7.0 g) underwent further separation using column chromatography, with silica gel G_{60} as the stationary phase (70 - 230 mesh) and a gradient elution of *n*-hexane acetate (1 %). This process yielded 5 subfractions (D1 - D5). Subfraction D4 was

subsequently separated by column chromatography with a methylene chloride acetate gradient elution (0.1 %), resulting in four subfractions (D4a - D4d). From subfraction D4d (0.02 g), further column chromatography using silica ODS and 100 % methanol as the eluent yielded compounds **1** (10.2 mg) and **2** (4.5 mg). Similarly, fraction E (8.23 g) was separated by VLC using silica G_{60} and an *n*-hexane acetate gradient (3 %), yielding seven subfractions (E1 - E7). Subfraction E3 was recrystallized in methanol to obtain compound **3** (6.3 mg).

Determination of cytotoxicity

Cytotoxic activity was assessed using methods adapted from prior research [23]. The MCF-7 breast cancer cell line was cultured in RPMI 1640 medium supplemented with 10 % fetal bovine serum (FBS) and an antibiotic-streptomycin solution (100 µg/mL). Cells were seeded into 96-well plates and incubated for 48 h at 37 °C with 5 % CO_2 to promote cell adhesion and proliferation. Different concentrations of the test samples, dissolved in dimethyl sulfoxide (DMSO), were applied to the wells. Cisplatin served as the positive control, while DMSO was used as the negative control. Following 48 h of incubation, PrestoBlue reagent was added to each well, and plates were incubated for another 1 - 2 h. The absorbance was measured at 570 nm using a multimode reader. The IC_{50} value, representing the concentration required to inhibit 50 % of cell growth, was determined by plotting the sample concentration against the percentage of viable cells, with PBS and DMSO used as controls.

Results and discussion

The results of compound isolation

Elucidation of compound 1

The compound **1** was obtained as colourless crystals, soluble in chloroform and exhibited an HRTOF-MS spectrum (**Figure 1**) with a positive ion peak at m/z 465.4037 $[M+Na]^+$ (calculated for $C_{30}H_{50}O_2Na$, m/z 465.3709), leading to the molecular formula $C_{30}H_{50}O_2$. This suggested that the compound belongs to the triterpenoid class with a degree of unsaturation (DBE) of 6. The IR spectrum (**Figure 2**) displayed absorption bands for a hydroxyl group (3,423 cm^{-1}), CH sp^3 (2,936 cm^{-1}), C=C (1,708 cm^{-1}) and gem-dimethyl (1,384 and 1,364 cm^{-1}).

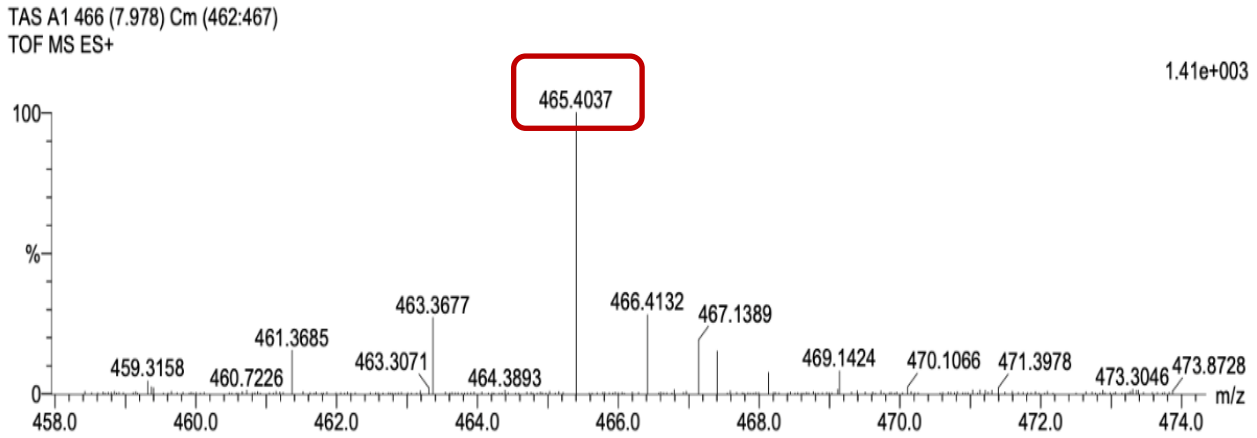

Figure 1 High-Resolution Time-of-Flight Mass Spectrometry (HRTOF-MS) Spectrum of Compound **1**; Key peaks are labeled, indicating the molecular ion (M+) and significant fragment ions. The spectrum illustrates the high-resolution capability of the instrument, highlighting the accurate mass measurements that support the identification of compound **1**.

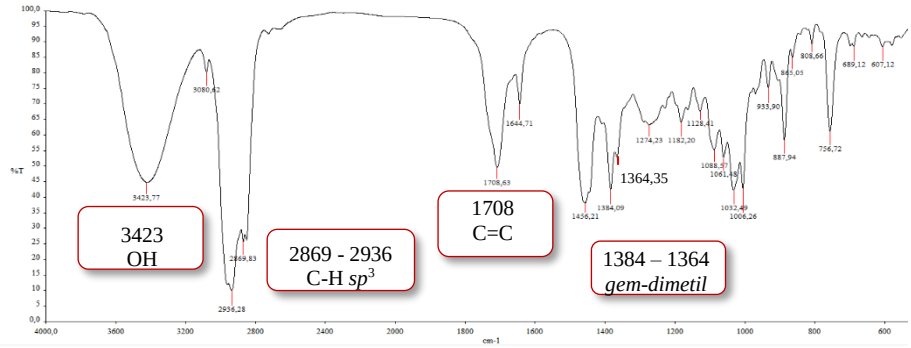

Figure 2 Fourier Transform Infrared (FTIR) Spectrum of Compound **1**. The characteristic functional groups present in the compound based on their respective absorption peaks. The spectrum provides insights into the molecular structure and bonding characteristics of compound **1**.

The ^{1}H-NMR spectrum (**Figure 3**) of compound **1** (**Table 1**) revealed seven singlet signals for methyl groups, with six shielded methyl signals at δ_H 0.67 (3H, s, H-25); 0.70 (3H, s, H-28); 0.76 (3H, s, H-24); 0.83 (3H, s, H-29); 0.96 (3H, s, H-30); 0.99 (3H, s, H-23) and one more deshielded methyl group at δ_H 1.69 (3H, s, H-27), indicating the presence of a methyl group attached to a quaternary carbon. Additionally, sp^2 methylene groups were observed at δ_H 4.54 (1H, s, H-26a) and 4.84 (1H, s, H-26b), corresponding to signals for an olefin group. Further, signals for oxygenated protons appeared at δ_H 3.26 (2H, dd, H-3; H-21), and a sp^2 methine signal was observed at δ_H 5.38 (1H, brs, H-15), which is characteristic of an olefinic group.

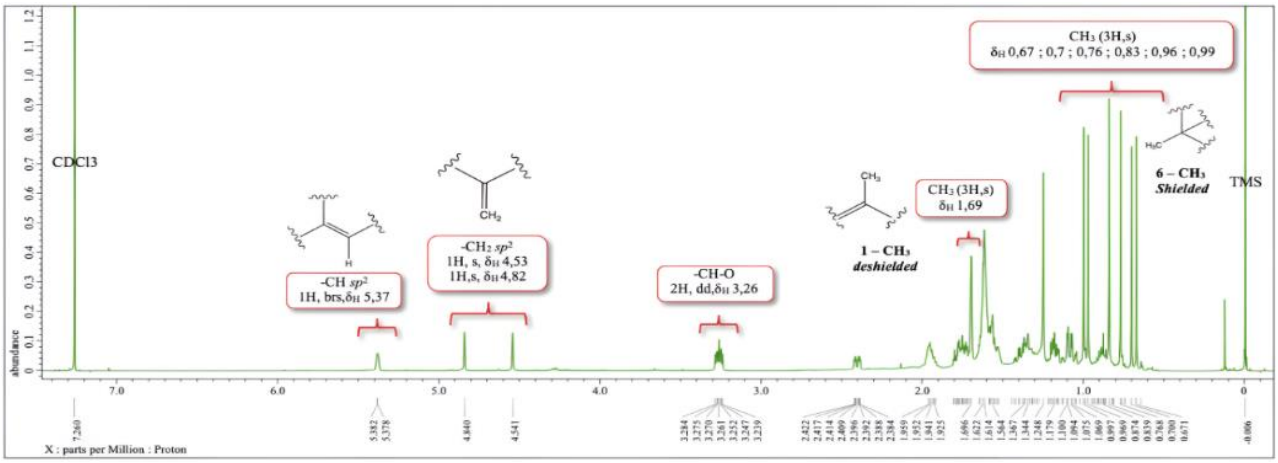

Figure 3 ^{1}H NMR spectrum (7,500 MHz, $CDCl_3$) of compound **1;** serves as a vital tool for confirming the structure of compound **1**, aiding in the identification of functional groups and the overall connectivity of the molecular framework. The distinct peaks and their patterns offer insights into the chemical behavior of the protons, further solidifying the characterization of this compound.

The ^{13}C-NMR spectrum, along with DEPT-135 ° (**Figure 4**) and HMQC spectra (**Figure 5**), identified 30 carbon signals consisting of seven sp^3 methyl groups (δ_C 28.0, 15.4, 14.7, 22.4, 13.6, 15.1 and 28.3 ppm), nine sp^3 methylene groups (δ_C 37.2, 27.5, 25.3, 38.2, 25.8, 23.5, 24.0, 29.4 and 28.0 ppm), one sp^2 methylene group (δ_C 106.8 ppm), four sp^3 methine groups (δ_C 49.7, 54.7, 57.1 and 55.3 ppm), one sp^2 methine group (δ_C 121.9 ppm), two oxygenated sp^3 methine groups (δ_C 79.2 and 78.9 ppm), four sp^3 quaternary carbons (δ_C 38.7, 36.5, 39.3 and 39.2 ppm) and two sp^2 quaternary carbons (δ_C 135.5 and 148.2 ppm). This analysis suggested that compound **1** has a secogamacera skeleton, supported by the DBE

value of 6 derived from two double bonds and four cyclic structures.

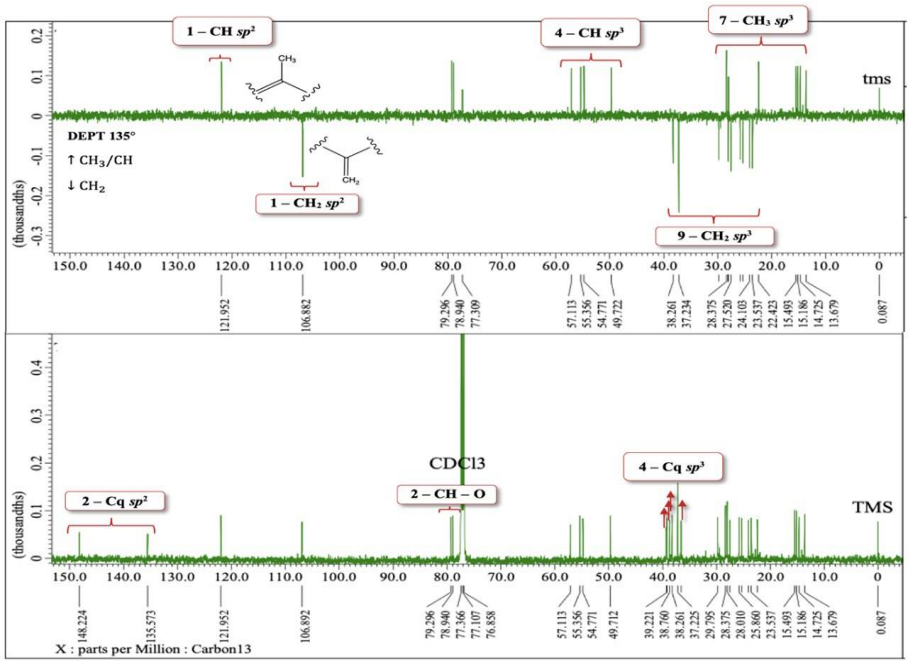

Figure 4 ^{13}C NMR and DEPT 135 spectrum (175 MHz, $CDCl_3$) of compound **1**; displayed to provide detailed information on the carbon framework and the type of carbon atoms present in the molecule. The DEPT 135 technique differentiates between methyl, methylene and methine carbon atoms.

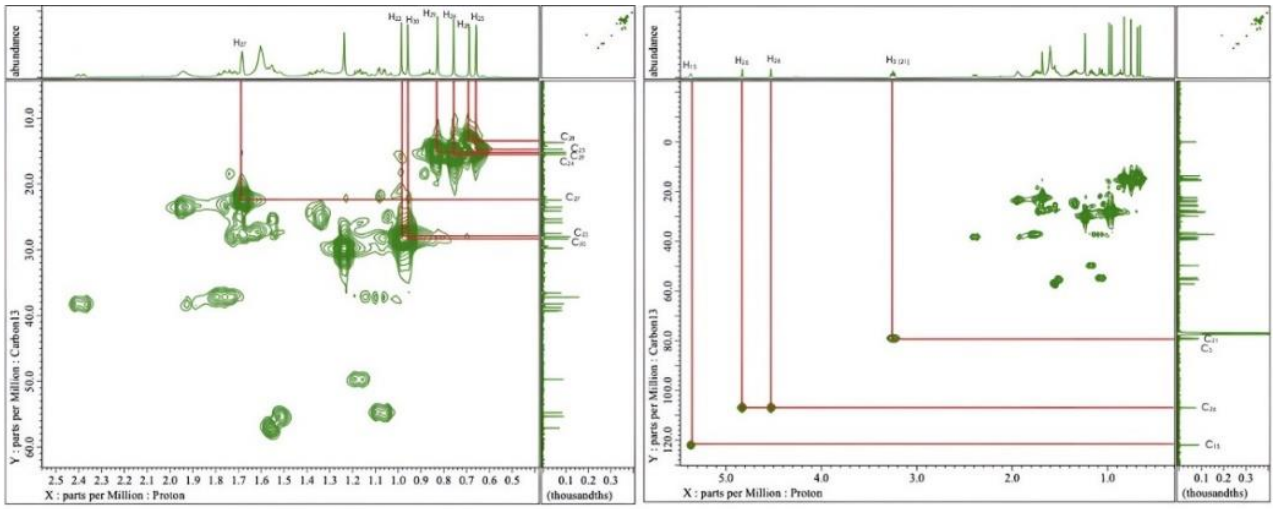

Figure 5 Heteronuclear Multiple Quantum Coherence (HMQC) spectrum of compound **1**.

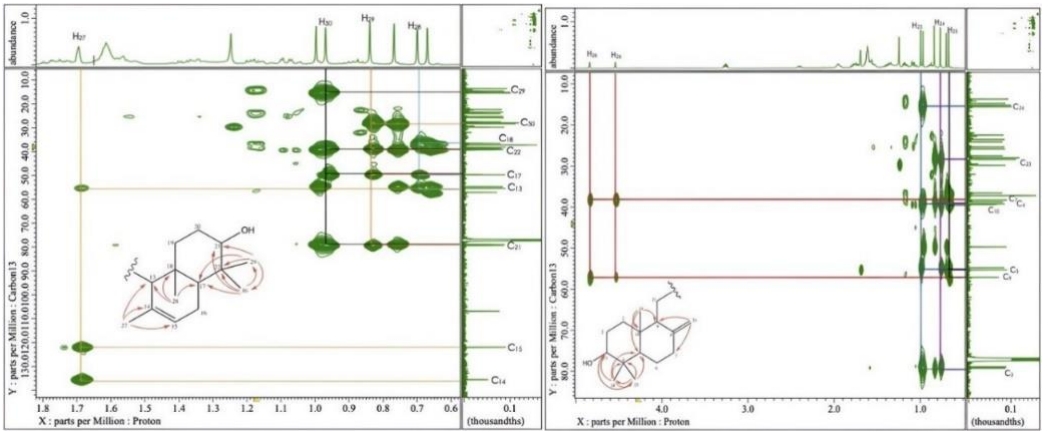

Figure 6 Heteronuclear Multiple Bond Correlation (HMBC) spectrum of compound **1**; instrumental in confirming the structural framework of compound **1** by elucidating the long-range interactions between protons and carbons.

This prediction was reinforced by HMBC and ^{1}H-^{1}H COSY spectra analyses (**Figures 6** and **7**). In this compound, correlations were observed between H-25 and C-10/C-5/C-9, H-24 and C-23/C-4/C-5/C-3, as well as between H-23 and C-24/C-4/C-5/C-3. Another correlation occurred between H-26 and C-7/C-9, confirming the position of the double bond at C-26. The analysis of these correlations reveals the relationship between rings A and B at C-5. Additional correlations were found between H-27 and C-14/C-15/C-13, H-29 and C-30/C-21/C-22/C-17, as well as between H-30 and C-29/C-21/C-22/C-17. Furthermore, the correlation of H-28 with C-18/C-13/C-17 indicates that the tertiary methyl group (C-28) is attached to C-18, which neighbours C-13 and C-17.

In the ^{1}H-^{1}H COSY spectrum, cross peaks were observed between H-1 and H-2 and between H-2 and H-3, confirming that C-1 and C-3 are each connected to C-2. Additional correlations were found between H-5/H-6/H-7 and H-9/H-11/H-12/H-13, resulting in a ring system composed of rings A and B connected to ring C. Other correlations include H-15/H-16/H-17 and H-19/H-20/H-21, leading to a ring system for ring C connected to ring D.

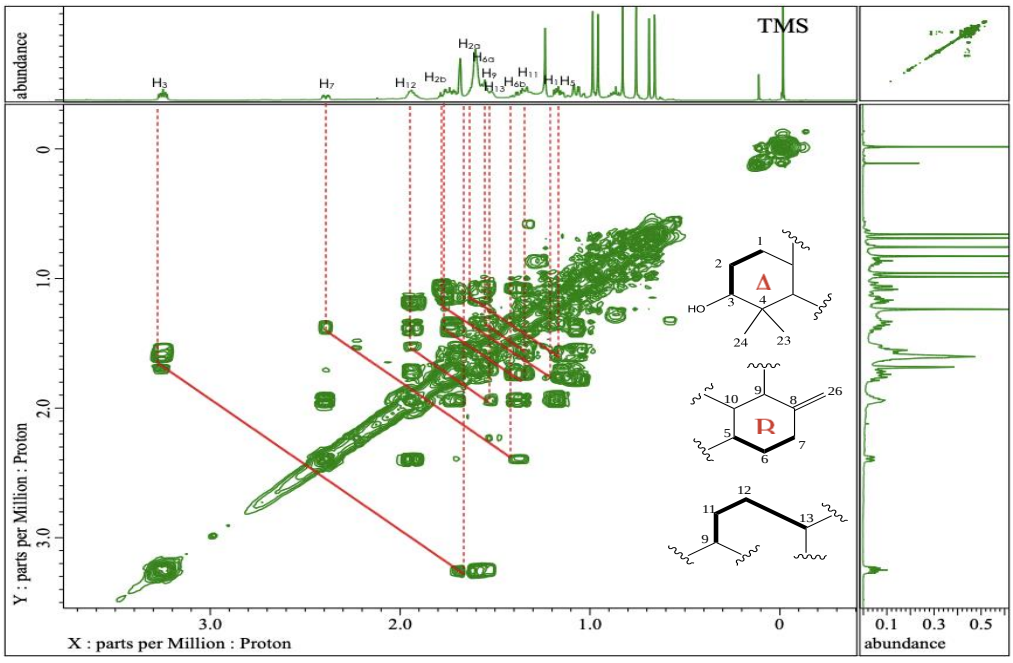

Figure 5 ^{1}H-^{1}H Correlation spectroscopy spectrum of compound **1**; displays correlations between protons that are directly connected (typically 1 or 2 bonds apart).

The configuration of this compound was further supported by the NOESY spectrum (**Figure 8**). The NOESY spectrum shows a key correlation between H-3 and H-5, which suggests that these protons are spatially close and on the same plane. Since H-5 is known to be *β*-oriented in many triterpenoids, this implies that H-3 is also β-oriented, placing the hydroxyl group at C-3 in the *β* orientation (since the proton and hydroxyl group are on opposite sides of the plane). The NOESY correlations provide strong evidence for the configuration of the hydroxyl groups at C-3 and C-21, and stereochemistry at C-9, while comparison to known triterpenoid structures helps infer the stereochemistry at C-13. This explanation ties together the spatial relationships observed in NOESY with established stereochemical patterns for triterpenoids. The overall comparison of the spectral data and literature suggests [21] that compound **1** is 8,14-sekogamasera-8(26),14-die*n*-3,21-diol, which was isolated for the first time from *Lansium domesticum*, in which this compound was the outcome of the reduction (synthesis) of compound **3** conducted by Nishizawa *et al.* [22]. The overall structural correlations of compound **1** based on the HMBC spectrum can be seen in **Figure 9**.

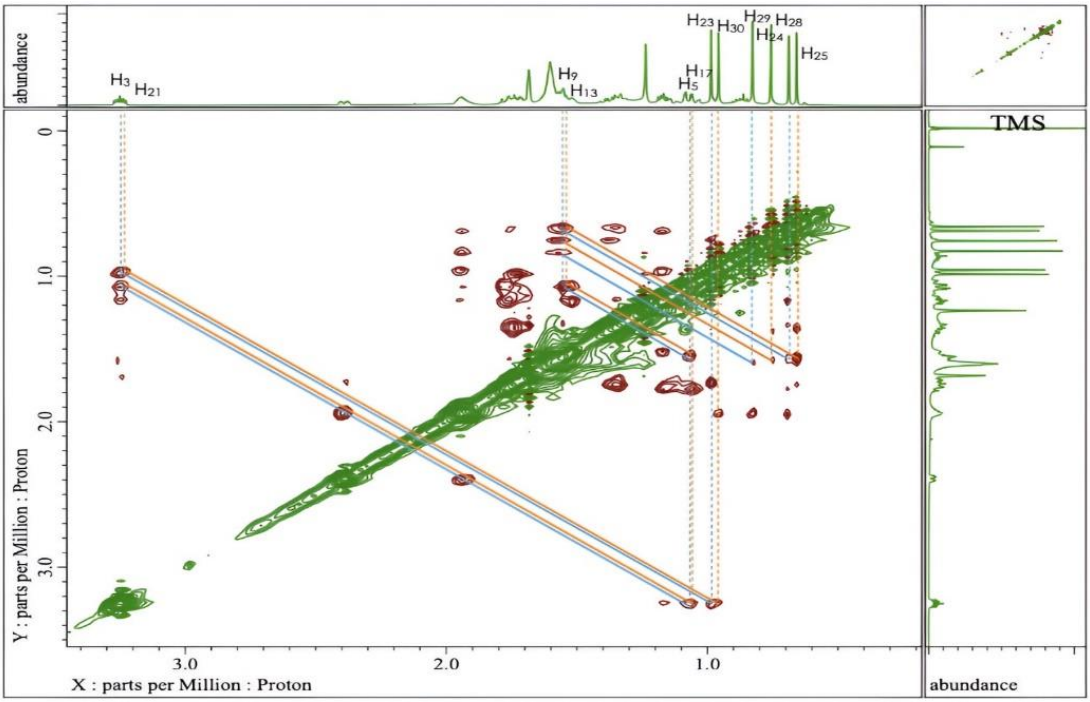

Figure 6 Nuclear Overhauser Effect Spectroscopy (NOESY) spectrum of compound 1; provides valuable information about spatial relationships between protons that are not directly bonded but are in close proximity (typically within 4 Å).

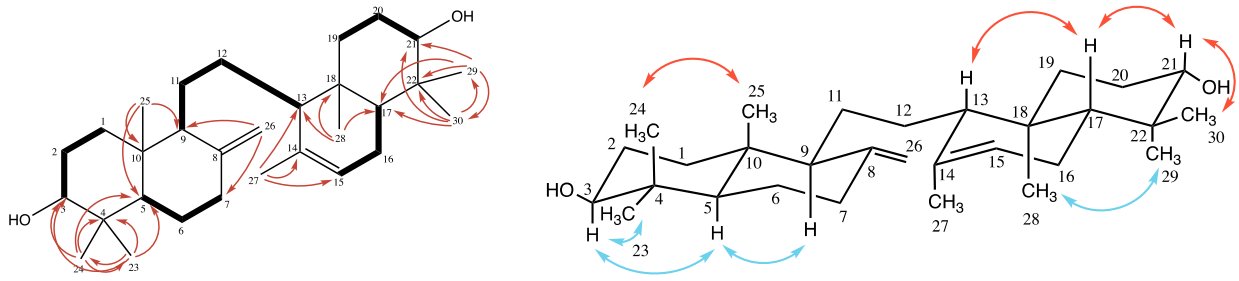

Figure 9 Selected ^{1}H-^{1}H COSY and HMBC correlations of **1** (a) and NOESY correlations of **1** (b).

Elucidation of compound 2

Compound **2** was an oil that is soluble in chloroform. Compound **2** was measured using HRTOF-MS ES+ and showed a peak with a value of m/z 441.3729 [M + H^+] (Calc. of m/z 441.3733) (**Figure 10**). Compound **2** was suspected to be a compound with the molecular formula $C_{30}H_{48}O_2$ and has a degree of unsaturation (DBE) of seven, derived from one carbonyl, two double bonds and four cyclics. The infrared (IR) spectrum (**Figure 11**) of compound **2** exhibited characteristic absorptions at 3,457 cm^{-1} for OH stretching vibration, 3,080 cm^{-1} for C-H *sp²* stretching, 2,938 cm^{-1} for C-H *sp³* stretching, 1,708 cm^{-1} for a carbonyl group (ketone), 1,455 cm^{-1} for a C=C bond, 1,385 cm^{-1} for a gem-dimethyl group and 1,269 cm^{-1} for a C-O group.

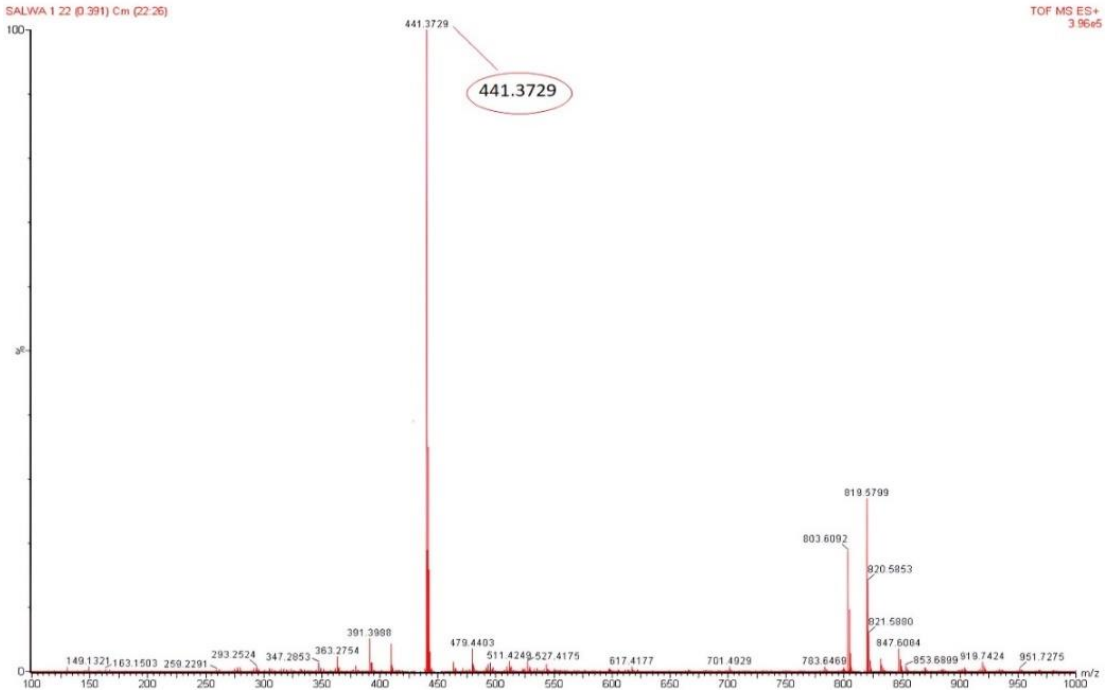

Figure 10 The High-Resolution Time-of-Flight Mass Spectrometry (HRTOF-MS) spectrum of compound **2**.

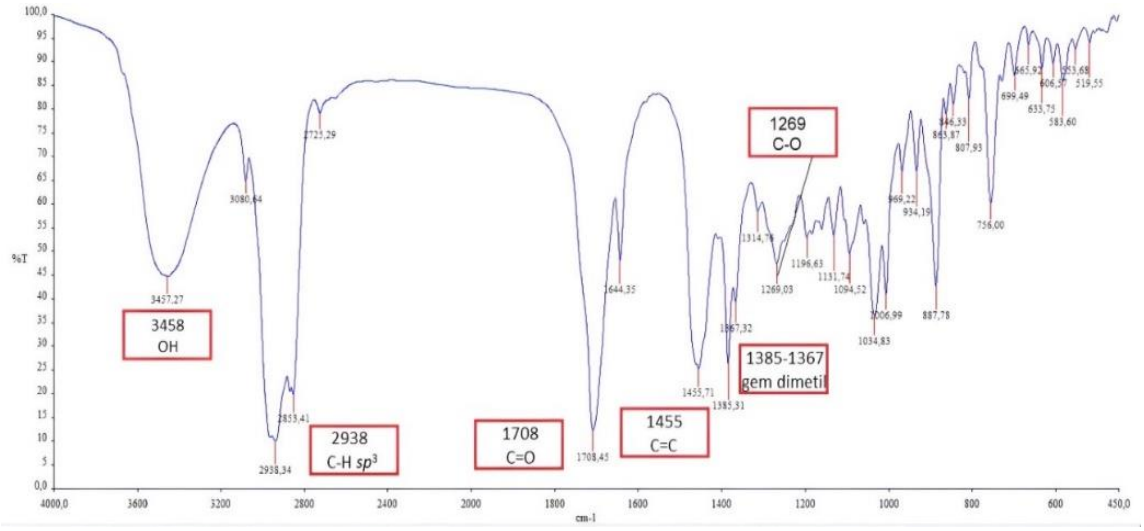

Figure 11 Fourier Transform Infrared (FTIR) spectrum of compound **2**.

The ^{1}H-NMR spectrum (**Figure 12**) of compound **2** revealed the presence of 7 singlet methyl signals at δ_H 0.64, 0.74, 0.91, 0.97, 1.02, 1.06, 1.07 and 1.69 ppm, indicating the presence of gem-dimethyl groups substituted at C-4 and C-22. A multiplet signal for an oxygenated proton appeared at δ_H 3.29 ppm, suggesting the presence of an OH group substituted at C-3. Two singlet signals for protons attached to *sp²* carbon atoms were observed at δ_H 4.52 and 4.82 ppm, corresponding to the olefinic protons at C-26. Additionally, a broad singlet signal at δ_H 5.39 ppm (1H) was identified as an olefinic methine proton at C-15, which was further supported by the IR spectrum indicating the presence of olefinic groups. The presence of these 2 olefinic groups strongly suggests that compound **2** is a triterpenoid of the onoceranoid type.

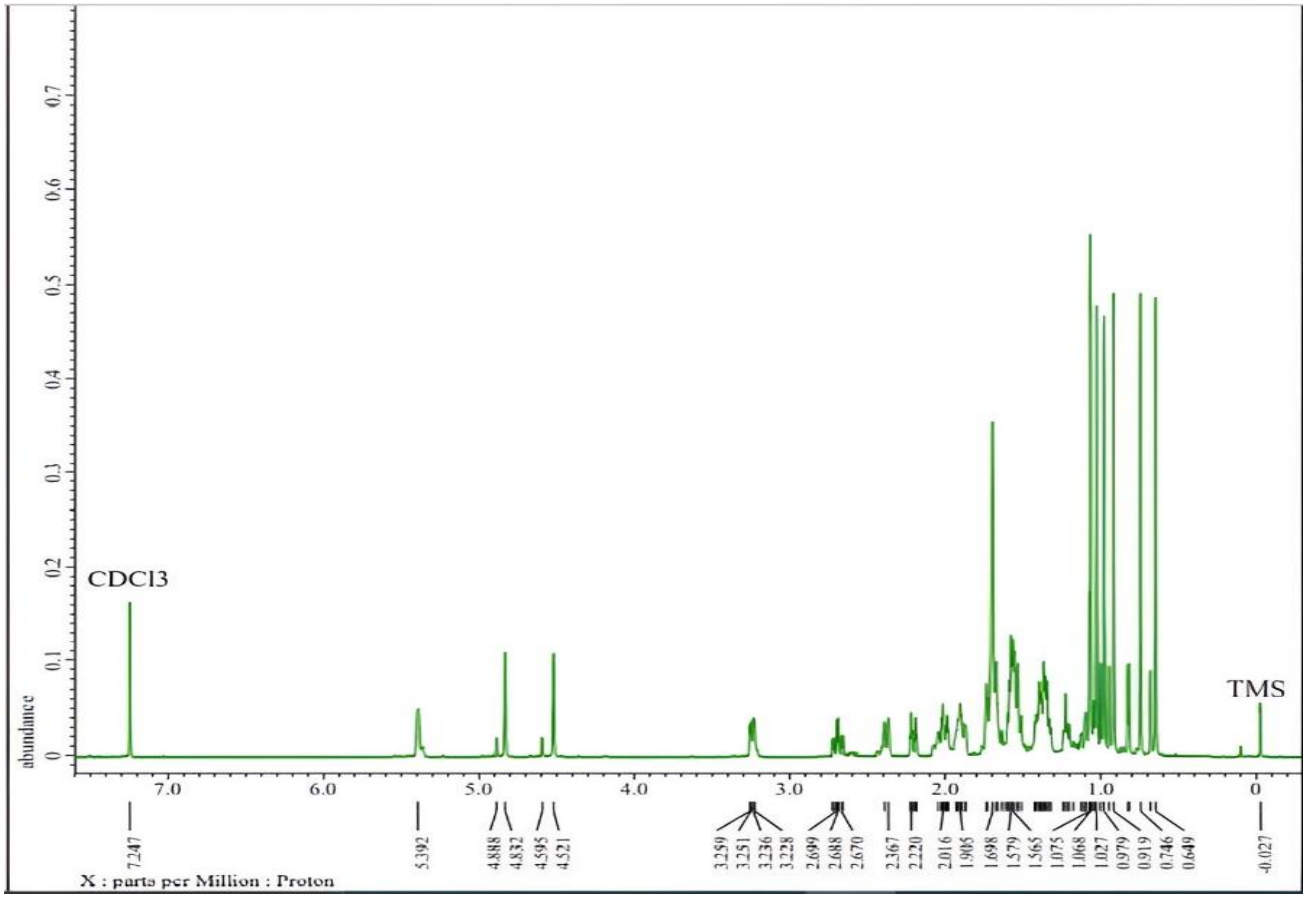

Figure 12 ^{1}H NMR spectrum (7,500 MHz, CDCl3) of compound **2**.

The ^{13}C-NMR and DEPT 135 ° spectra (**Figure 13**) of compound **2** revealed the presence of 30 carbon signals, a characteristic feature of triterpenoids. These signals include 7 methyl groups [δ_C (ppm) 13.3, 14.6, 15.4, 22.1, 22.2, 24.9 and 28.2], some of which are associated with gem-dimethyl groups, a hallmark of onoceranoid triterpenoids. Additionally, 10 methylene groups were observed [δ_C (ppm) 23.9, 24.0, 24.8, 25.5, 27.9, 34.7, 37.2, 38.0, 38.1 and 106.9], 5 *sp³* methine groups [δ_C (ppm) 51.5, 54.3, 54.7, 56.6 and 79.5], 1 *sp²* methine group [δ_C 121.7 ppm], three *sp³* quaternary carbons [δ_C 39.1, 39.2 and 36.4 ppm] and four *sp²* quaternary carbons [δ_C 47.5, 135.8, 148.1 and 217.3 ppm]. The ^{13}C-NMR spectrum displayed several carbon signals typical of triterpenoids. The four *sp²* carbon signals at δ_C 106.9, 148.1, 135.8 and 121.7 ppm indicated the presence of double bonds substituted at C-8 and C-26, as well as C-14 and C-15, which aligned with the IR spectrum's indication of double bonds. A distinctive signal at δ_C 79.5 corresponded to an oxygenated carbon bonded to an -OH group, while the signal at δ_C 217.3 ppm represented a C=O group. The presence of a C=O group at δ_C 217.3 and olefinic signals at δ_C 106.9, 148.1, 135.8 and 121.7 suggested that

compound **2** is a tetracyclic triterpenoid. The analysis of the ^{13}C-NMR spectrum indicates that compound **2** has a secogamaserane framework, with ^{1}H-NMR and ^{13}C-NMR chemical shifts similar to those of 3*β*-hydroxyonocera-8(26),14-dien-21-one, in which this compound was the outcome of the reduction (synthesis) of compound **3** conducted by Nishizawa *et al.* [22].

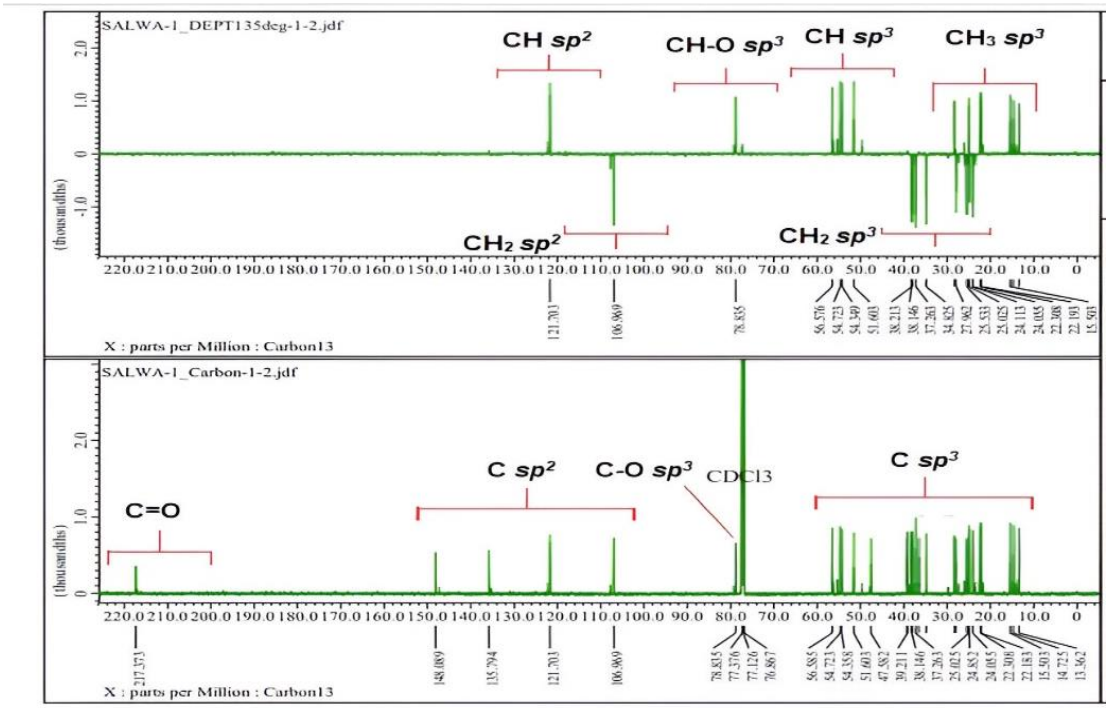

Figure 13 ^{13}C NMR and DEPT 135 spectrum (175 MHz, $CDCl_3$) of compound **2**.

Elucidation of compound 3

Compound **3** was obtained as a colorless solid. The molecular weight of **3** that was acquired from the HRTOF-MS spectrum (**Figure 14**) was 439.3358 $[M + H]^+$ (calculated 439.3396), and the molecular formula prediction of compound **3** was $C_{30}H_{47}O_2$. The IR spectrum (**Figure 15**) presented the existence of 3,080 cm^{-1} for C-H *sp²* stretching, 2,935 cm^{-1} for C-H *sp³* stretching, 1,709 cm^{-1} for a carbonyl group (ketone), 1,456 cm^{-1} for a C=C bond and 1,385 cm^{-1} for a gem-dimethyl group.

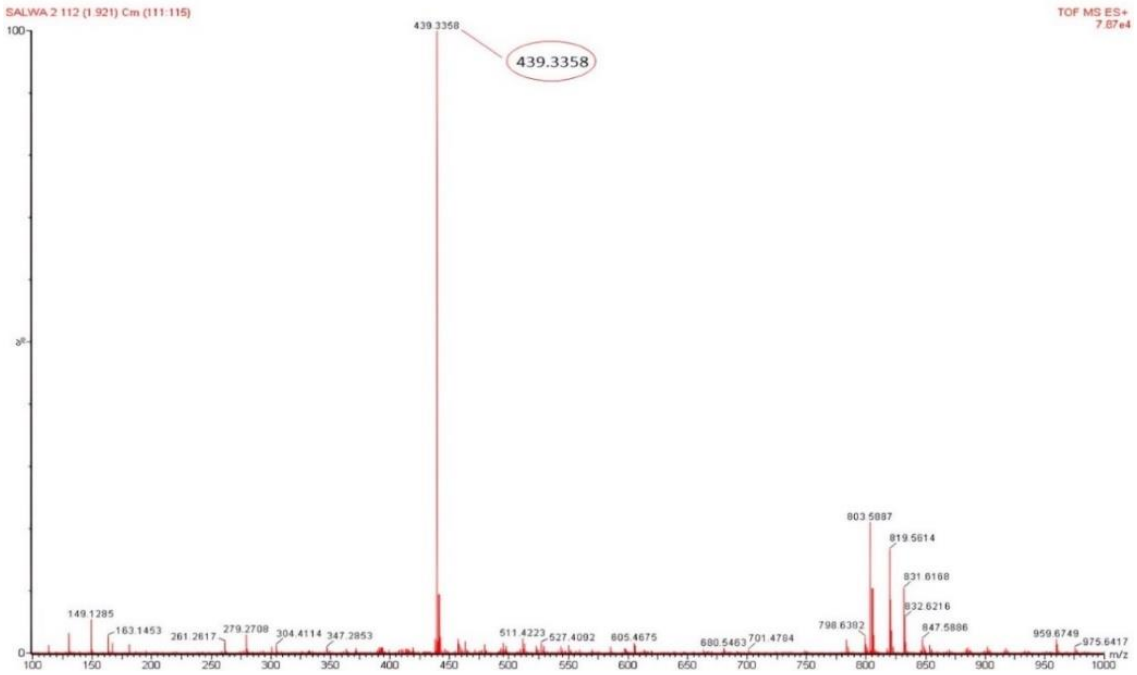

Figure 14 HRTOF-MS spectrum of compound **3**.

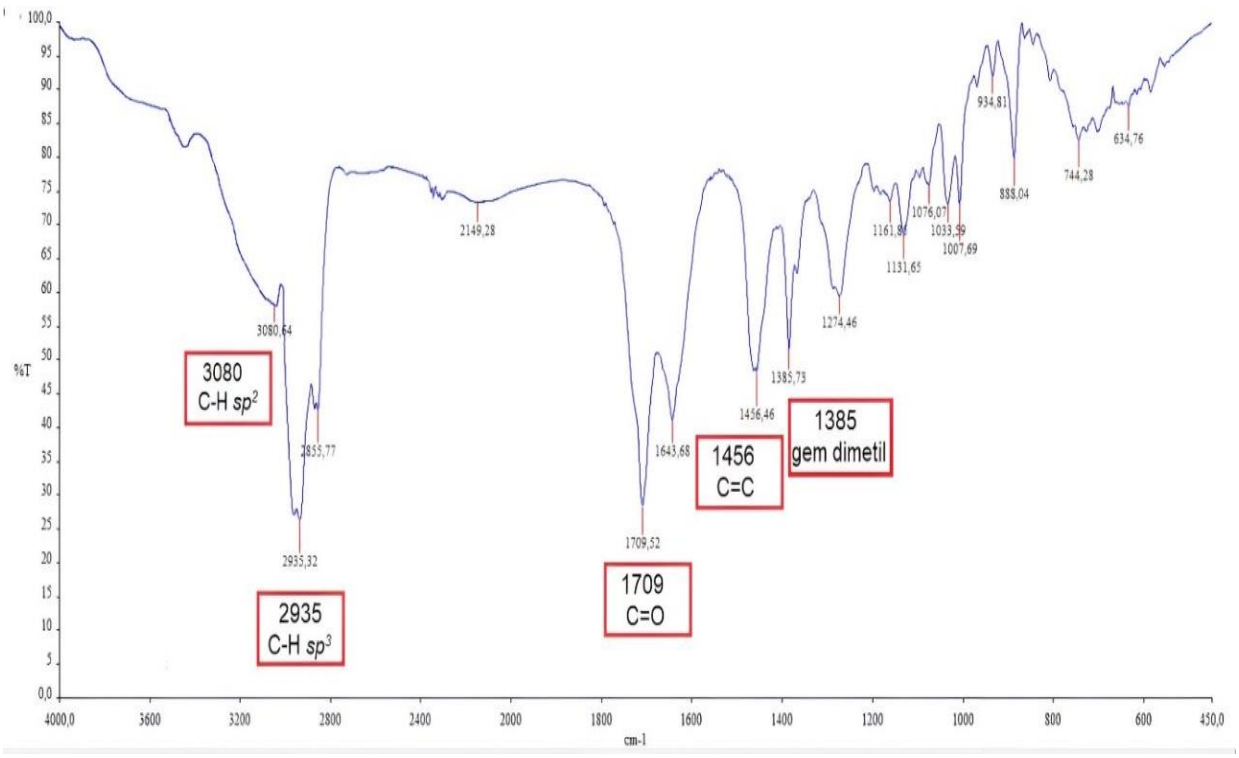

Figure 15 FTIR spectrum of compound **3**.

The ^{1}H-NMR ($CDCl_3$ 500 MHz) (**Figure 16**) and ^{13}C-NMR, DEPT 135 ° spectra (**Figure 17**) of compound **2** denoted that compound **2** had a similar structural framework to compound **2**, but compound **3** did not have a hydroxy group, as evidenced by the absence of hydroxy wave absorption in its IR spectrum. This indicated that compound **3** at C-3 was bonded to a carbonyl group. This prediction was confirmed by the appearance of 2 carbonyl groups at δ_C shifts of 207.1 and 217.3 ppm. Compound **3**, which has been identified as

α,γ-onoceradienedione and is depicted in **Figure 18**, agreed well with data from the literature [21,24].

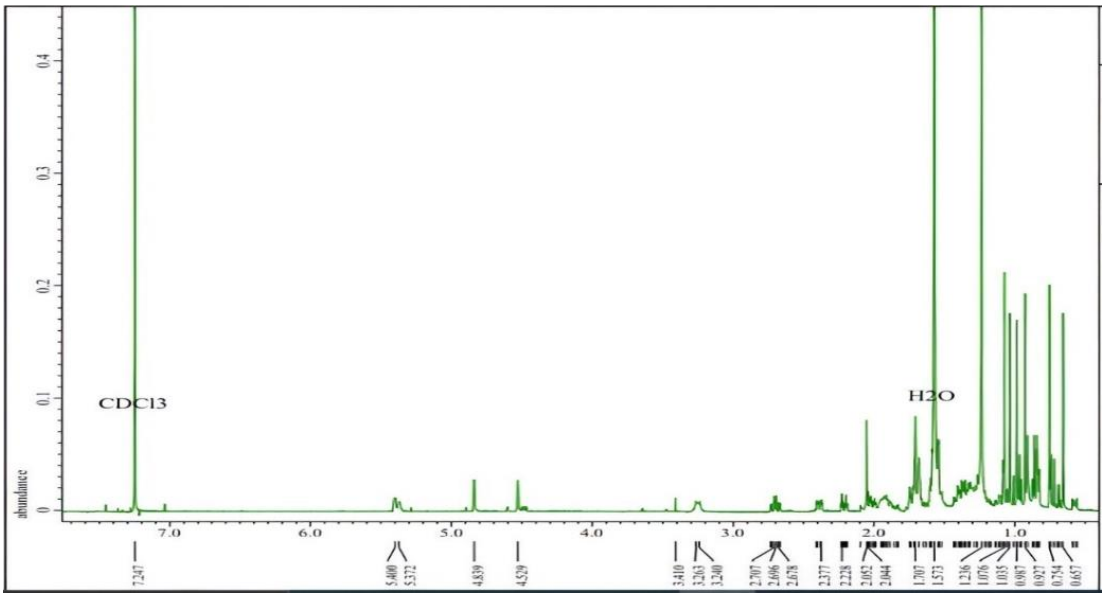

Figure 16 ^{1}H NMR spectrum (7500 MHz, $CDCl_3$) of compound **3**.

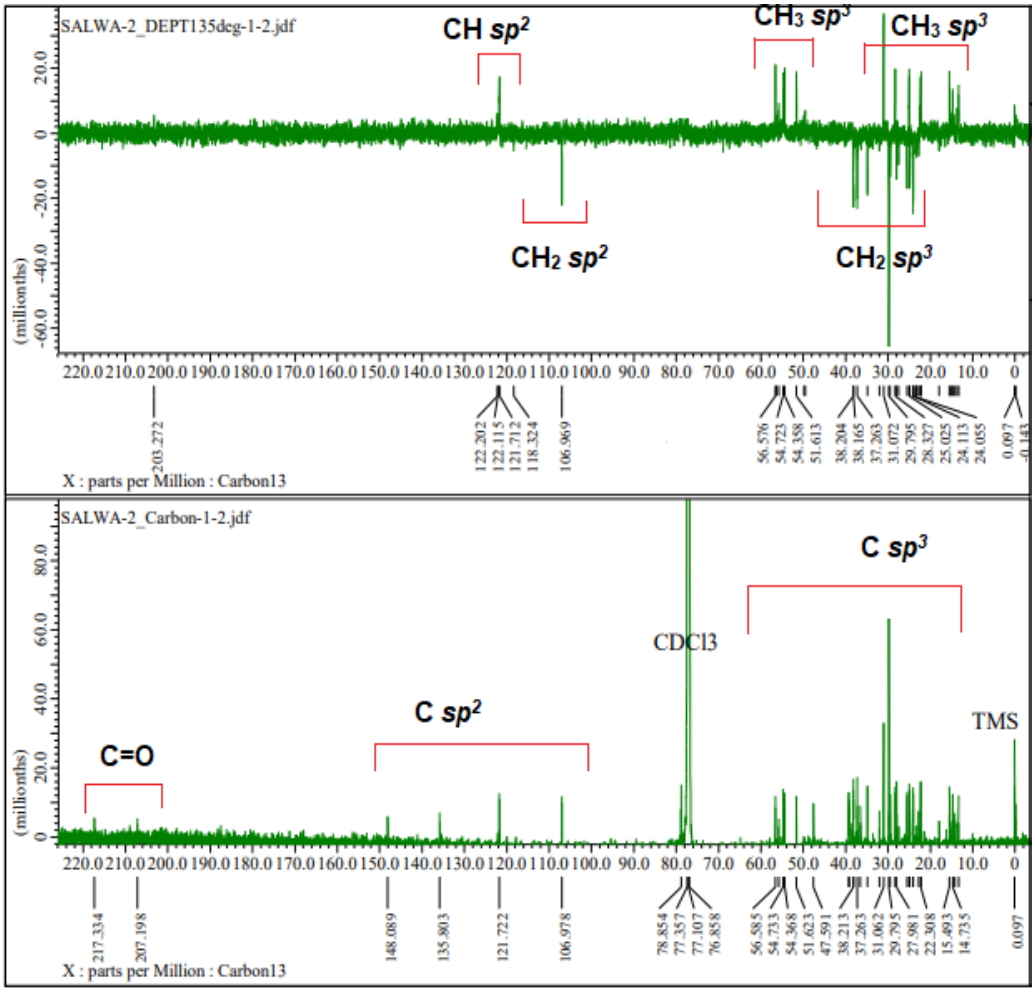

Figure 17 ^{13}C NMR and DEPT 135 spectrum (175 MHz, $CDCl_3$) of compound **3**.

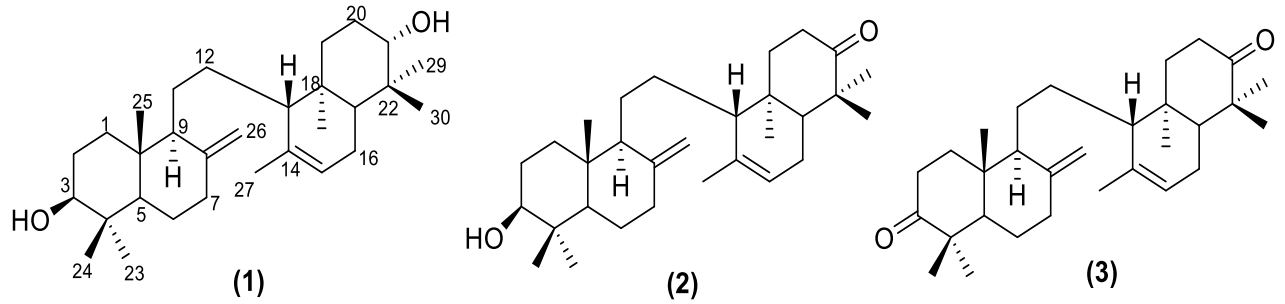

Figure 18 The structure of compounds **1** - **3**.

Table 1 NMR data (500 MHz for ^{1}H and 125 MHz for ^{13}C, in $CDCl_3$) for **1** - **3**.0

Position	1		2		3	
	^{13}C NMR δ_C	**^{1}H NMR δ_H (Σ H mult, J = Hz)**	**^{13}C NMR δ_C**	**^{1}H NMR δ_H (Σ H mult, J = Hz)**	**^{13}C NMR δ_C**	**^{1}H NMR δ_H (Σ H mult, J = Hz)**
1	37.2	1.17 (1H, m), 1.80 (1H, m)	37.2	1.20 (1H, m), 1.87 (1H, m)	37.2	1.23 (1H, m), 1.82 (1H, m)
2	27.5	1.62 (1H, m), 1.70 (1H, m)	27.9	1.75 (1H, m), 1.61 (1H, m)	27.9	1.58 (1H, m), 1.70 (1H, m)
3	79.2	3.25 (1H, dd), 11.5, 4.0	78.8	3.26 (1H, dd), 11.5, 4	207.2	-
4	39.2	-	39.2	-	39.2	-
5	55.3	1.16 (1H, m)	54.7	1.13 (1H, m)	54.7	1.08 (1H, m)
6	25.3	1.62 (1H, m), 1.40 (1H, m)	24.8	1.66 (1H, m), 1.42 (1H, m)	24.8	1.63 (1H, m), 1.40 (1H, m)
7	38.2	1.95 (1H, m), 2.3 (1H, m)	38.1	1.98 (1H, m), 2.07 (1H, m)	38.1	1.99 (1H, m), 2.03 (1H, m)
8	148.2	-	148	-	148	-
9	57.1	1.57 (1H, m)	56.5	1.57 (1H, m)	56.5	1.57 (1H, m)
10	39.3	-	39.2	-	39.2	-
11	25.8	1.34 (2H, m)	25.5	1.20 (2H, m)	25.5	1.28 (2H, m)
12	23.5	1.79 (1H, m), 1.96 (1H, m)	24	1.87, 2.18 (2H, m)	24.1	1.88, 2.19 (2H, m)
13	54.7	1.55 (1H, m)	54.3	1.66 (1H, m)	54.3	1.64 (1H, m)
14	135.5	-	135.8	-	135.8	-
15	121.9	5.38 (1H, brs)	121.7	5.39 (1H, brs)	121.7	5.40 (1H, brs)
16	24.0	1.42 (1H, m), 1.94 (1H, m)	24.1	1.42 (1H, m), 1.97 (1H, m)	24.0	1.40 (1H, m), 1.98 (1H, m)
17	49.7	1.15 (1H, m)	51.6	1.67 (1H, m)	51.6	1.64 (1H, m)
18	36.5	-	36.5	-	36.2	-
19	29.4	1.18 (1H, m), 1.39 (1H, m)	38.2	1.58 (1H, m), 2.46 (1H, m)	38.2	1.40 (1H, m), 2.46 (1H, m)
20	28.0	1.65 (1H, m), 1.77 (1H, m)	34.8	2.26 (1H, m), 2.73 (1H, m)	34.8	2.22 (1H, m), 2.73 (1H, m)
21	78.9	3.25 (1H, dd), 11.5, 4.0	217.3	-	217.3	-
22	38.7	-	47.5	-	47.6	-
23	28.0	0.99 (3H, s)	28.3	0.97 (3H, s)	28.3	0.98 (3H, s)

Position	1		2		3	
	^{13}C NMR δ_C	^{1}H NMR δ_H (Σ H mult, J = Hz)	^{13}C NMR δ_C	^{1}H NMR δ_H (Σ H mult, J = Hz)	^{13}C NMR δ_C	^{1}H NMR δ_H (Σ H mult, J = Hz)
24	15.4	0.76 (3H, s)	15.5	0.75 (3H, s)	15.5	0.75 (3H, s)
25	14.7	0.67 (3H, s)	14.7	0.68 (3H, s)	14.7	0.65 (3H, s)
26	106.8	4.84 (1H, s), 4.54 (1H, s)	106.9	4.82 (1H, s), 4.52 (1H, s)	106.9	4.83(1H, s), 4.52 (1H, s)
27	22.4	1.69 (3H, s)	22.3	1.70 (1H, m)	22.3	1.70 (1H, m)
28	13.6	0.7 (3H, s)	13.3	0.92 (3H, s)	13.3	0.92 (3H, s)
29	15.1	0.83 (3H, s)	22.1	1.07 (3H, s)	22.1	1.07 (3H, s)
30	28.3	0.96 (3H, s)	24.9	1.03 (3H, s)	25.0	1.03 (3H, s)

The NMR data of the 3 compounds were compiled into **Table 1**, which presented a comparison of the 3 compounds.

The cytotoxicity of compounds (1 - 3)

Compounds **1-3** were evaluated against MCF-7 cell lines and the result can be seen in **Table 2**. The structure-activity relationship (SAR) of the compounds (**1** - **3**) can be understood by examining the structural features that influence their cytotoxic activity against MCF-7 cancer cells. Compound (**1**) contains 2 hydroxyl groups at C-3 and C-21. This compound showed the lowest cytotoxic activity with an IC_{50} value greater than 150 µg/mL. The presence of multiple hydroxyl groups might increase hydrophilicity, which could reduce the compound's ability to interact with hydrophobic sites within the cancer cell membrane [25,26]. In contrast, compound (**2**) exhibited strong cytotoxic activity with an IC_{50} value of 17.11 µg/mL. This compound features a hydroxyl group at C-3, a carbonyl group at C-21. The presence of the carbonyl and hydroxyl groups likely enhances the molecule's ability to form hydrogen bonds, which may improve its binding affinity to biological targets, including proteins or enzymes in cancer cells [27]. Compound (**3**) is structurally similar to compound (**2**) but includes an additional carbonyl group at C-3. It has an IC_{50} value of 19.66 µg/mL, slightly less active than compound (**2**). The additional carbonyl group might alter the electronic distribution across the molecule, potentially affecting its binding affinity and slightly reducing its cytotoxic activity compared to compound (**2**). Compounds (**2**) and (**3**), with more hydrophobic characteristics and fewer hydroxyl groups, show better cytotoxicity than compound (**1**), suggesting that a balanced hydrophilicity-hydrophobicity profile is crucial for optimal cytotoxic activity against MCF-7 cancer cells.

Table 2 Cytotoxicity activity of compounds **1** - **3** against MCF-7 cancer lines [28].

Compound	Cytotoxicity (IC_{50}, µg/mL)	Activity
1	> 150	Inactive
2	17.11	Strongly active
3	19.66	Strongly active
Cisplatin (positive control)	15.96	Strongly active

Conclusions

In conclusion, this study successfully isolated and characterized 3 onoceranoid triterpenes from the ethyl acetate extract of kokosan cultivar fruit peels of *Lansium domesticum*. The identified compounds, 8,14-secogammacera-8(26),14-dien-3,21-diol (**1**), 3β-hydroxyonocera-8(26),14-dien-21-one (**2**), and α,γ-onoceradienedione (**3**), are noteworthy, particularly as compounds **1** and **2** represent novel contributions to the understanding of this genus, previously synthesized from compound **3**. The *in vitro* cytotoxicity results highlight compound **2** as the most potent against MCF-7 breast cancer cells, followed closely by compound **3**, while compound **1** exhibited negligible activity. The promising anticancer properties of compounds **2** and **3**, comparable to the standard drug cisplatin, underscore their potential for further therapeutic development. Looking ahead, the findings pave the way for several important research directions. Future studies should prioritize *in vivo* investigations to assess the efficacy and safety of these compounds in a living organism. Additionally, exploring the underlying mechanisms of action will provide deeper insights into their anticancer effects and could inform the development of targeted therapies. Ultimately, this research contributes to the broader quest for novel anticancer agents derived from natural products, offering hope for innovative treatment strategies in oncology.

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