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New Alkamides from Maca (*Lepidium meyenii*)

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Maca (*Lepidium meyenii*) has been used as a food in Peru for thousands of years. More recently a wide array of commercial maca products have gained popularity as dietary supplements, with claims of anabolic and aphrodisiac effects, although the biologically active principles are not fully known. In an earlier chemical investigation, two new alkamides and a novel fatty acid, as well as the *N*-hydroxypyridine derivative, macaridine, were isolated from *L. meyenii*. Further examination has led to the isolation of five additional new alkamides, namely, *N*-benzyl-9-oxo-12*Z*-octadecenamide (**1**), *N*-benzyl-9-oxo-12*Z*,15*Z*-octadecadienamide (**2**), *N*-benzyl-13-oxo-9*E*,11*E*-octadecadienamide (**3**), *N*-benzyl-15*Z*-tetracosenamide (**4**), and *N*-(*m*-methoxybenzyl)hexadecanamide (**5**). Their structures were established by spectrometric and spectroscopic methods including ESI-HRMS, EI-MS, ^{1}H, ^{13}C, and 2D NMR, as well as ^{1}H−^{15}N 2D HMBC experiments. In addition, the identity of *N*-benzyl-15*Z*-tetracosenamide (**4**) was confirmed by synthesis. These compounds have been found from only *L. meyenii* and could be used as markers for authentication and standardization.

KEYWORDS: **Maca; *Lepidium meyenii*; Brassicaceae; alkamide; macamide**

INTRODUCTION

Maca, *Lepidium meyenii* Walpers (Brassicaceae), a perennial herbaceous plant found on high plateaus of the Andean mountain area in Peru, is an important dietary staple for the indigenous people (*1*). The tuberous root of maca is generally consumed fresh or dried, having a tangy taste and an aroma similar to that of butterscotch. In South America, maca tubers are used to make porridge, jam, and pudding. In Peru, they are often made into a sweet, fragrant fermented drink called maca chichi. According to folk belief, maca can enhance sexual drive and female fertility in humans and domestic animals. It is also reputed to have properties that include regulation of hormonal secretion, immunostimulation, memory improvement, antidepressant, anticancer, and effectiveness for curing anemia, menstrual, and sexual disorders (*1*, *2*). Due to these putative virtues, maca is also called “Peruvian ginseng”. However, these properties have not been clearly substantiated by scientific research.

On the basis of maca’s long history and traditional use, a wide array of commercial maca products are currently gaining popularity as dietary supplements throughout the world, with claims of anabolic and aphrodisiac effects. Several pharmacological studies carried out in recent years support such indications (*3*, *4*). Chemical investigations of maca led to the isolation of fatty acids, glucosinolates, sterols, and alkaloids (*5*−*7*). Even though the biologically active principles of maca are not fully known, the hexane extract of maca tubers showed promising biological activities (*8*, *9*).

In our earlier investigations (*10*, *11*), two new alkamides, macamides **6** and **7** (**Figure 1**), and a novel fatty acid, macaene, as well as the *N*-hydroxypyridine derivative, macaridine, were isolated from maca hexane extract. In the current study, we undertook the isolation and identification of additional new alkamides.

MATERIALS AND METHODS

General Apparatus and Chemical. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX-500 instrument at 500 MHz (^{1}H) and 125 MHz (^{13}C), using the residual solvent signal as internal standard; multiplicity determinations (DEPT 135) and 2D NMR spectra (COSY, NOESY, HMQC, and HMBC) were acquired using standard Bruker pulse programs; ^{15}N NMR spectra were recorded at 50.7 MHz with chemical shift relative to liquid NH_3 by calibrating nitromethane to 380.2 ppm; HRMS spectra were obtained by direct injection using a Bruker Bioapex-FTMS with electrospray ionization (ESI) source; EI-MS was carried out on a Hewlett-Packard 5989B GC-MS spectrometer. TLC was performed with silica gel 60 GF_{254} plates (EM Science) and a solvent of CH_2Cl_2/EtOAc (8:2). Flash-silica gel, 40 μm (J. T. Baker), Sephadex LH-20 (Amersham Biosciences), and flash cartridges (Horizon HPFC system, Biotage, Inc.) were used for column chromatography. UV spectra were recorded on a Hewlett-Packard 8453 UV−vis spectrometer. IR spectra were recorded on an ATI Mattson Genesis series FTIR spectrometer.

Plant Material. The tubers of *L. meyenii* were purchased from American Mercantile Cooperation, Memphis, TN, in 2000. A voucher specimen (voucher LAMEB 2384) has been deposited at the Herbarium of The University of Mississippi.

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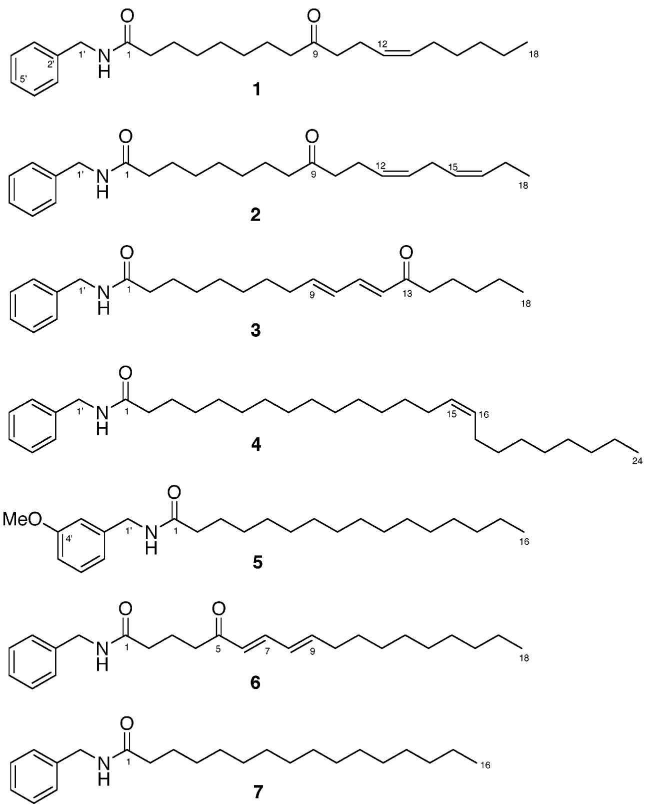

Figure 1. Structures of alkamides from maca (*L. meyenii*).

Isolation and Identification. *L. meyenii* dried ground tubers (2 kg) were percolated at room temperature with 95% EtOH, and the solvent was evaporated under reduced pressure to yield 435 g of crude extract. The hexane-soluble portion (21 g) of the EtOH extract was subjected to Si gel (40 μM) column chromatography, eluted by $CHCl_3$ followed by increasing concentrations of EtOAc (0−100%) in $CHCl_3$ to give 15 fractions, which were pooled by TLC characteristics. Fraction 3 (780 mg), fraction 5 (1.02 g), and fraction 7 (745 mg) were then chromatographed on Sephadex LH-20 columns eluted with CH_2Cl_2, to afford fraction 3-A (**4** enriched), fraction 5-B (**5** enriched), fraction 7-B (**1** enriched), and fraction 7-C (mixture of **2** and **3**), respectively. These fractions were separated and purified by using the HRFC chromatography system (Biotage, Inc.), with Flash 12+M cartridges, EtOAc/hexane, and diethyl ether/hexane, to afford compounds **1** (8 mg), **2** (6 mg), **3** (4 mg), **4** (7 mg), and **5** (16 mg).

N-Benzyl-9-oxo-12Z-octadecenamide (1): white powder; UV (MeOH) λ_{max} (log ϵ) 212 (3.88), 274 (2.98) nm; IR (film) ν_{max} 3310 (N−H), 2925, 2827, 1629, 1543, 1415, 1233, 677 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz), see **Table 1**; ^{13}C NMR ($CDCl_3$, 125 MHz), see **Table 2**; HRESIMS, *m/z* found 386.3020 ($[M + H]^+$), calcd for $C_{25}H_{40}NO_2$ $[M + H]^+$, 386.3054.

N-Benzyl-9-oxo-12Z,15Z-octadecadienamide (2): white powder; UV (MeOH) λ_{max} (log ϵ) 210 (3.96), 274 (3.18) nm; IR (film) ν_{max} 3311 (N−H), 2925, 2855, 1636, 1545, 1237, 998, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz), see **Table 1**; ^{13}C NMR ($CDCl_3$, 125 MHz), see **Table 2**; HRESIMS, *m/z* found 384.2906 ($[M + H]^+$), calcd for $C_{25}H_{38}NO_2$ $[M + H]^+$, 384.2902.

N-Benzyl-13-oxooctadeca-9E,11E-dienamide (3): gum; UV (MeOH) λ_{max} (log ϵ) 208 (4.02), 276 (4.04) nm; IR (film) ν_{max} 3312 (N−H), 2928, 2849, 1681,1638, 1594, 1546, 1239, 1001, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz), see **Table 1**; ^{13}C NMR ($CDCl_3$, 125 MHz), see **Table 2**; HRESIMS, *m/z* found 384.2912 ($[M + H]^+$), calcd for $C_{25}H_{38}NO_2$ $[M + H]^+$, 384.2902.

N-Benzyl-15Z-tetracosenamide (4): white powder; UV (MeOH) λ_{max} (log ϵ) 212 (3.86) nm; IR (film) ν_{max} 3295 (N−H), 2916, 2846, 1637, 1549, 1458, 1235, 721, 696 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz), see **Table 1**; ^{13}C NMR ($CDCl_3$, 125 MHz), see **Table 2**; EIMS, *m/z* 455 $[M^+]$, 412, 398, 370, 356, 342, 330, 316, 302, 218, 162, 149, 106, 91, 55; HRESIMS, *m/z* found 456.4151 ($[M + H]^+$), calcd for $C_{31}H_{54}NO$ $[M + H]^+$, 456.4199.

N-(m-Methoxybenzyl)hexadecanamide (5): white powder; UV (MeOH) λ_{max} (log ϵ) 216 (3.94), 274 (3.41) nm; IR (film) ν_{max} 3294 (N−H), 2921, 2850, 1640, 1534, 1461, 1261, 1154, 1049, 776, 692 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz), see **Table 1**; ^{13}C NMR ($CDCl_3$, 125 MHz),

Table 1. ^1H NMR Data [δ in Parts per Million, *J* in Hertz] of Compounds **1**–**5** (500 MHz, $CDCl_3$)[a]

proton	1	2	3	4	5
2	2.22 t (7.6)	2.21 t (7.6)	2.21 t (7.6)	2.23 t (7.6)	2.22 t (7.6)
3	1.65 m	1.66 m	1.65 m	1.67 m	1.66 m
4–6	1.29 m*	1.29 m*	1.29 m*	1.29 m*	1.30 m*
7	1.57 m	1.56 m	1.43 m	1.30 m*	1.30 m*
8	2.38 t (7.2)	2.37 t (7.2)	2.16 m	1.30 m*	1.30 m*
9			6.14 m	1.30 m*	1.30 m*
10	2.43 t (7.2)	2.45 t (7.2)	6.15 m	1.30 m*	1.30 m*
11	2.30 dt	2.33 dt	7.12 dd (15.6, 3.2)	1.30 m*	1.30 m*
12	5.30 dt	5.35 dt	6.06 d (15.6)	1.30 m*	1.30 m*
13	5.41 dt	5.40 m		1.31 m*	1.30 m*
14	2.03 m	2.79 dd (6.8, 6.8)	2.53 t (7.2)	2.03 m	1.29 m*
15	1.33 m	5.29 dt	1.60 m	5.37 m	1.28 m
16	1.28 m	5.39 m	1.28 m	5.37 m	0.90 t (7.6)
17	1.29 m	2.07 dq	1.30 m	2.03 m	
18	0.88 t (7.6)	0.96 t (7.6)	0.90 t (7.6)	1.31 m*	
19–22				1.30 m*	
23				1.28 m	
24				0.90 t (7.6)	
1′	4.45 d (5.6)	4.43 d (5.6)	4.43 d (5.6)	4.46 d (5.6)	4.41 d (5.6)
3′	7.29 m	7.26 m	7.26 m	7.29 m	6.82 dd
4′	7.35 m	7.31 m	7.32 m	7.35 m	
5′	7.28 m	7.24 m	7.25 m	7.28 m	6.83 m
6′	7.35 m	7.31 m	7.32 m	7.35 m	7.26 dt
7′	7.28 m	7.24 m	7.25 m	7.29 m	6.86 d (7.6)
OMe					3.80 s
NH	5.83 br s	5.76 br s	5.78 br s	5.78 br s	5.90 br s

[a] An asterisk (*) indicates superimposition with other CH_2 protons.

Table 2. ^{13}C NMR Data (δ in Parts per Million) of Compounds **1**–**5** (125 MHz, $CDCl_3$)[a]

carbon	1	2	3	4	5
1	173.0 s[b]	172.9 s	172.9 s	173.4 s	173.1 s
2	36.7 t	36.7 t	36.7 t	37.8 t	36.8 t
3	25.6 t	25.6 t	25.7 t	26.8 t	25.8 t
4–6	29.1 t*	29.1 t*	29.1 t*	30.7 t*	29.4 t*
7	23.6 t	23.7 t	29.2 t	30.6 t*	29.5 t*
8	42.8 t	42.9 t	33.1 t	30.6 t*	29.5 t*
9	210.9 s	210.7 s	145.8 d	30.6 t*	29.5 t*
10	42.7 t	42.5 t	128.9 d	30.6 t*	29.5 t*
11	21.7 t	21.7 t	142.9 d	30.6 t*	29.5 t*
12	127.7 d	128.1 d	127.8 d	30.5 t*	29.6 t*
13	131.2 d	129.3 d	201.2 s	30.3 t*	29.7 t*
14	27.2 t	25.5 t	40.5 t	28.2 t	31.9 t
15	29.3 t	127.0 d	24.7 t	130.5 d	22.7 t
16	31.5 t	132.1 d	31.6 t	130.5 d	14.1 q
17	22.6 t	20.6 t	22.5 t	28.2 t	
18	14.1 q	14.3 q	14.0 q	30.3 t*	
19–21				30.6 t*	
22				32.9 t	
23				23.7 t	
24				15.2 q	
1′	43.6 t	43.6 t	43.6 t	44.5 t	43.5 t
2′	138.4 s	138.4 s	138.4 s	139.0 s	140.1 s
3′	127.8 d	127.8 d	127.8 d	128.4 s	112.9 d
4′	128.7 d	128.7 d	128.7 d	129.3 d	159.9 s
5′	127.5 d	127.5 d	127.5 d	128.1 d	113.3 d
6′	128.7 d	128.7 d	128.7 d	129.3 d	129.7 d
7′	127.8 d	127.8 d	127.8 d	128.4 d	120.0 d
OMe					55.2 q

[a] An asterisk (*) indicates superimposition with other CH_2 carbons. [b] Multiplicities were determined by DEPT, also aided by 2D NMR COSY and HMQC experiments.

see **Table 2**; HRESIMS, m/z found 376.3174 ([M + H]$^+$), calcd for $C_{24}H_{42}NO_2$ [M + H]$^+$, 376.3210.

Synthesis of *N*-Benzyl-15*Z*-tetracosenamide (4). Benzylamine (32.14 mg, 0.3 mmol) and *cis*-15-tetracosenoic acid (73.2 mg, 0.2 mmol) were dissolved in dry methylene chloride (3 mL), and a catalytic amount of (dimethylamino)pyridine was added to this solution. The reaction mixture was stirred at room temperature under a nitrogen atmosphere for 20 min. Dicyclohexyl carbodiimide (61.8 mg, 0.3 mmol) was added to the above reaction mixture, and the reaction was stirred at the same temperature. The progress of the reaction was monitored by silica gel TLC, which showed the formation of one product, completed in 90 min. The solid dicyclohexyl urea formed was removed by filtration, and the filtrate was dried under reduced pressure at 20 °C. The semisolid mass was subjected to silica gel column chromatography (*n*-hexane/ethyl acetate, 1:1) to give the pure desired product. The EI-MS, NMR, UV, and IR data of this synthetic product were identical with those observed for *N*-benzyl-15*Z*-tetracosenamide (**4**).

RESULTS AND DISCUSSION

The hexane-soluble portion of the EtOH extract of *L. meyenii* tubers was fractionated and purified by multistep chromatographies to obtain alkamides **1**−**5**.

Compound **1** was obtained as a white powder, and its molecular formula was determined as $C_{25}H_{39}NO_2$ by ESI-HRMS. The ^{1}H NMR spectrum demonstrated five aromatic protons (δ 7.28−7.34, 5H, m) (**Table 1**), which were correlated to carbon signals at δ_C 128.7 (CH × 2), 127.8 (CH × 2), and 127.5 (CH) in the ^{1}H−^{13}C HMQC spectrum. These were attributed to a monosubstituted benzene ring. A doublet methylene proton signal (H-1′) at δ_H 4.45 (J = 5.6 Hz) demonstrated a strong ^{1}H−^{1}H coupling to the NH proton (δ_{N-H} 5.83, confirmed by a ^{1}H−^{15}N NMR HMBC experiment) and very weak ^{1}H−^{1}H couplings with benzene protons in the COSY spectrum, and correlations to three carbons of the benzene ring (C-2′, C-3′, and C-7′) and a carbonyl carbon (δ_C 173.0) from the ^{1}H−^{13}C HMBC spectrum suggested the presence of an *N*-benzyl amide fragment. This was further supported by ^{1}H−^{15}N NMR HMBC experiments in which the ^1J, ^2J, and ^3J correlations between N (δ_N 120.1) and the proton N−H, H-1′, and H-2 were observed. These signals were found to be very similar to those reported for alkamides **6** and **7** (*10*). The IR spectra of compound **1** revealed the informative absorption bands at around ν_{max} 3310, 1629, 1233, and 677 cm^{-1} due to N−H, carbonyl, and benzene groups, respectively.

The ^{1}H, ^{13}C, and DEPT NMR spectra of **1** demonstrated that it possessed a straight alkyl chain and contained a ketone group with the ^{13}C chemical shifts at 210.9, as well as one double bond indicated by olefinic proton signals at δ_H 5.41 and 5.30 and corresponding alkene carbon signals at δ_C 127.7 and 131.2. According to the DQF-COSY and HMBC spectra, a straight-chain moiety of $-CH_2CH_2COCH_2CH_2CH{=}CHCH_2CH_2CH_2$-$CH_2CH_3$ was established. This moiety was further connected to the foregoing *N*-benzyl amide fragment through five methylene groups. Thus, all proton and carbon signals of compound **1** were assigned, and its structure was identified as *N*-benzyl-9-oxo-12*Z*-octadecenamide. The geometry of the double bond was determined to be cis, as evidenced by the chemical shifts of carbons C-11 (δ_C = 21.7) and C-14 (δ_C = 27.2). Usually, the signals of carbons next to a cis double bond appear at δ_C 27−28, whereas those of a trans double bond appear at δ_C 32−33 (*12*, *13*). The upfield shift of the C-11 carbon signal is attributed to the shielding effect of the nearby carbonyl group. This cis alkene bond configuration was also supported by the NOE interaction between H-11 and H-14 observed in the NOESY spectrum.

Compound **2** gave a molecular formula of $C_{25}H_{37}NO_2$ based on the ESI-HRMS, which was 2 mass units lower compared to **1**. The ^{1}H and ^{13}C NMR spectra of **2** showed marked similarity with those of **1**. Five aromatic proton signals were attributed to a monsubstituted bezene ring, and the same was true for the presence of an *N*-benzyl amide fragment as in compound **1**. In addition, it also contained a ketone group (δ_C 210.7). The differences were that compound **2** had two double bonds, corresponding to the olefinic proton signals between δ_H 5.29 and 5.40 and carbon signals at δ_C 127.0, 128.1, 129.3, and 132.1. On the basis of the DQF-COSY and HMBC spectra, a linear chain linking of $-CH_2CH_2COCH_2CH_2CH{=}CHCH_2CH{=}CHCH_2CH_3$ was established in which a ketone and two double-bond groups are involved. This moiety is further connected to the *N*-benzyl amide fragment in the same way as for compound **1**. The geometries of the two double bonds were determined to be both cis, by the chemical shifts of carbon C-11 (δ_C 21.7), C-14 (δ_C 25.5), and C-17 (δ_C 20.6) adjacent to the double bonds. The chemical shift data of C-14 and C-17 were in agreement with those of corresponding carbons reported for (9*E*,12*Z*,15*Z*)-linolenic acid (*13*). Accordingly, the structure of **2** was established as *N*-benzyl-9-oxo-12*Z*,15*Z*-octadecadienamide.

The ^{1}H and ^{13}C NMR spectra of **3** were generally similar to those observed for **1** and **2**. An *N*-benzyl amide fragment was identified, which showed almost the same ^{1}H and ^{13}C NMR data as those in **1** and **2**. Compound **3** has the same molecular formula, $C_{25}H_{37}NO_2$, as that of **2** according to ESI-HRMS measurement. Four olefinic protons with signals at δ_H 6.06, 6.14, 6.15, and 7.12, correlating to four carbons at δ_C 127.8, 145.8, 128.9, and 142.5, respectively, in the HMQC spectrum, indicated the presence of two double bonds. In addition, one ketone was recognized from the ^{13}C chemical shift at δ_C 201.2. The downfield shifts of the signals for the two double bonds and the carbonyl group suggested that they were conjugated. According to the DQF-COSY and HMBC spectra, the locations of the ketone and two double bonds were determined, and a linear chain linked as $-CH_2CH_2CH{=}CHCH{=}CHCOCH_2CH_2$-$CH_2CH_2CH_3$ was established. In the same way as for **1** and **2**, this moiety was further connected to the *N*-benzyl amide fragment through five methylene groups from the analysis of the HMBC spectrum. Accordingly, the structure of **3** was identified as *N*-benzyl-13-oxo-9*E*,11*E*-octadecadienamide. The geometries of the two double bonds were found to be both trans, as evidenced by the coupling constant (J = 15.6 Hz) between H-11 and H-12, as well as the chemical shift of C-8 (δ_C 33.1) next to the double bond. These configurations were supported by the observations of the NOE correlations between H-8 and H-10 and between H-9 and H-11, as well as between H-10 and H-12 from the NOESY experiment. The UV spectrum of **3** showed a strong absorption at λ_{max} = 276 nm (log ϵ = 4.04), which indicated the extended conjugation of the α,β-unsaturated ketone chromophore.

The ^{1}H and ^{13}C NMR spectra of compound **4** demonstrated a signal pattern of an *N*-benzyl amide moiety [Ph-CH_2NHCO−] similar to those of **1**−**3**. In the ^{1}H NMR spectrum, two olefinic protons exhibited a triplet signal at δ_H 5.37, which coupled with a multiplet signal of two methylene groups at δ_H 2.03 (−CH_2− × 2) in the COSY spectrum and showed correlation to the carbon signal at δ_C 130.5 (C × 2) in the HMQC spectrum. A triplet due to a methylene at δ_H 2.23 (J = 7.6 Hz) showed vicinal coupling to a methylene signal at δ_H 1.67 (m), and both of them gave ^{1}H−^{13}C HMBC correlations to the carbonyl carbon (δ_C 173.4). The remaining signals in the ^{1}H NMR spectrum were a primary methyl group at δ_H 0.90 and 32 protons with chemical shifts at around δ_H 1.30. These results suggested that there was a linear alkyl moiety with one double bond in the structure of **4**, which was then connected to the carbonyl of the *N*-benzyl amide fragment by the analysis of the HMBC spectrum. The ESI-HRMS of **4** gave the molecular formula as $C_{31}H_{53}NO$. Accordingly, the length of the acyl chain was determined and its structure was assigned as *N*-benzyltetracosenamide. The location of the double bond in the structure was determined to be at the C-15 position by the EI-MS spectra, which demonstrated characteristic fragment ions at *m*/*z* 356, 342, 330, and 316, caused by the α and β cleavages of the double bond (*14*). The geometry of the double bond was determined as cis, as shown by the chemical shifts of C-14 (δ_C 28.2) and C-17 (δ_C 28.2) adjacent to the double bond. Therefore, the structure of **4** was established as *N*-benzyl-15*Z*-tetracosenamide. *N*-Benzyl-15*Z*-tetracosenamide was synthesized from nervonic acid (*cis*-15-tetracosenoic acid) and benzylamine in our laboratory. The EI-MS, NMR, UV, and IR spectra and TLC of this synthetic product were identical to those of compound **4**.

The ^1H and ^{13}C NMR spectra of compound **5** exhibited similarities to the above four compounds. A carbonyl carbon (δ_C 173.1), a broad proton signal at δ_H 5.90, and a methylene group that gave a doublet proton signal at δ_H 4.41 and a carbon signal at δ_C 43.5, as well as the signal pattern of an alkyl chain, suggested it was also an alkamide. However, the signal pattern in the aromatic proton range of the ^1H NMR spectrum was different from those of compounds **1**−**4**. There were four aromatic protons with signals at δ_H 7.26 (dd, $J = 7.6$, 4.4 Hz, H-6′), δ_H 6.86 (d, $J = 7.6$ Hz, H-7′), δ_H 6.82 (H-5′), and δ_H 6.83 (H-3′), which were correlated to the carbon signals at δ_C 129.7, 120.0, 113.3, and 112.9, respectively, from the HMQC spectrum. These were assigned to a disubstituted benzene ring. A methoxyl group (δ_H 3.80, δ_C 55.2), which had a $^1H-^{13}C$ HMBC correlation to C-4′ (δ_C 159.9), was assigned to the meta position of this disubstituted benzene ring by the observation of the HMBC correlations from H-6′ (δ_H 7.26) to C-2′ (δ_C 140.1) and C-4′ (δ_C 159.9). All of this information indicated that compound **5** possesses an *N*-(*m*-methoxybenzyl) amide moiety. The remaining signals suggested a straight alkyl chain, of which one end was attached to the carbonyl group of the *N*-(*m*-methoxybenzyl) amide moiety revealed by the correlations of H-2 and H-3 to the carbonyl carbon C-1 from the HMBC spectrum. The HRMS of **5** gave the molecular formula as $C_{24}H_{41}NO_2$. Accordingly, the structure of compound **5** was assigned as *N*-(*m*-methoxybenzyl)hexadecanamide. Interestingly, its demethoxy analogue *N*-benzylhexadecanamide **7** (**Figure 1**) was isolated from *L. meyenii* and reported in our previous study (*10*).

This appears to be the first report of alkamides **1**−**5** from a natural source. Alkamides form a distinct class of natural products in which different amine parts are combined by an amide linkage with various fatty acids. They have restricted distributions in the plant kingdom, mainly in four plant families, Piperaceae, Aristolochiaceae, Rutaceae, and Asteraceae (*15*). It is intriguing to note that alkamides isolated from maca (Brassicaceae) are an exception to this systematic distribution, and they have not been reported even in other *Lepidium* species. Therefore, these compounds could be used as markers for authentication and standardization. All of these alkamides from *L. meyenii* appear to possess the amine moiety *N*-benzyl, whereas the acyl chains are unbranched, variable in lengths and unsaturation degrees, and sometimes contain a keto group.

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