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A trace alkaloid, oleraisoindole A from *Portulaca oleracea* L. and its anticholinesterase effect

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Abstract

A new trace alkaloid possessing the lignan structure, named oleraisoindole A, was obtained from the extract of the *Portulaca oleracea* L.. The structure of oleraisoindole A was elucidated by 1D and 2D NMR and high resolution electrospray ionization time-of-flight mass spectroscopic methods. The compound presented an anticholinesterase effect with the IC₅₀ value of 60.4 μ M.

Keywords: *Portulaca oleracea* L.; alkaloids; anticholinesterase effect

1. Introduction

Portulaca oleracea L., a member of the Portulacaceae family has been used as a vegetable, spice and medicine since the times of the ancient Egyptian and was popular in England during the Middle Ages 33 (Okafor et al. 2014). In China, *P. oleracea* is a traditional Chinese medicine well-known for its pharmacological function of removing heat, counteracting toxicity, cooling blood, hemostasia and antidysentery (The Pharmacopoeia Commission of PRC, 2015) owing to its many bioactive compounds, including alkaloids (Li et al. 2017; Xu et al. 2017; Zhao et al. 2018; Xiu et al. 2018), flavonoids (Yang et al. 2018; Yang et al. 2018), coumarins (Awad 1994), lignans (Ma et al. 2018), phenolic acids (Erkan 2012), terpenoids (Elkhayat et al. 2008). As alkaloids are the main components of the plant and presents many bioactivities, such as antiinflammatory (Meng et al. 2016; Jiang et al. 2018), antimalarial (Frederich et al. 2008) and antioxidant activities (Racková et al. 2004), etc.. Therefore, the aim of the study is to isolate alkaloids, a trace new alkaloid, named oleraisoindole A (Figure 1) was finally obtained from the extract of *P. oleracea*. In addition, its anticholinesterase effect was studied as Alzheimer's diseasehas (AD) related to acetylcholinesterase (AChE) (Howes et al. 2003).

Figure 1. Structure of Oleraisoindole A.

2. Results and discussion

Oleraisoindole A (1 mg, purity of > 99% with UHPLC) was obtained as a pale yellow powder, which turned orange and cyan after spraying Dragendorff reagent and ferric chloride on a TLC plate. UV-Vis (MeOH) λ_{max} : 284 nm. IR (KBr) ν_{max} : 3425, 1756, 1706, 1600, 1515, 1400, 1265, 1212 cm^{-1} . Its molecular formula was identified as $\text{C}_{28}\text{H}_{23}\text{NO}_7$ with 18 degrees of unsaturation based on a molecular ion peak at m/z 484.1404 $[\text{M}+\text{H}]^+$ in the HR-ESI-TOF-MS (calcd. for $\text{C}_{28}\text{H}_{23}\text{NO}_7$, 484.1401) and the NMR data (Table S1, in supplementary material). A 3-spin system was found, which linked to carbon C-4 at $\delta_{137.0}$ and defined a 1,3,4-trisubstituted phenyl moiety based on ^1H - ^1H coupling pattern, COSY and HMBC experiment. There is also a typical of *para*-disubstituted phenyl ring, in which C-2'' was linked to C-1''' as the HMBC spectrum shows the correlation H-2'''/C-2''. The ^1H - ^1H COSY and DEPT spectrum shows the correlation position 1'' ($\delta_{\text{H}}3.66$, $\delta_{\text{C}}39.0$)/2'' ($\delta_{\text{H}}2.74$, $\delta_{\text{C}}32.9$). The highfield chemical shift of position 2'' was obviously different with that of the oleraisoindole (Table S2 and Figure S1 in supplementary material) previously isolated in our lab (Jiang et al. 2018) meaning that CH_2 in oleraisoindole A only connected to position 1'' that was typical of CH_2 connected to N, and N linked to C-1 and C-3. In HMBC, H-1'' correlated to carbonyl groups C-1 and C-3 at $\delta_{166.9}$ and 167.4, respectively. In ^1H -NMR, only three singlet CH signals and nine quaternary carbons were remained and attached to the established peripheral groups. Protons H-8 and H-9 were not coupled to each other. Nevertheless, they correlated in ROE indicating that they were close to each other but not attached to a single phenyl ring. Altogether, these indications led to position two periprotons on a naphthalene moiety. Based on the strong ROE correlation between methyl group and H-8, the methoxy substituent at the C-7

position was determined. H-9 correlated to C-4a and H-8 which based on HMBC and ROE, respectively. This further confirms the relative positions of H-8 and H-9. H-9 also correlated to C-1 and C-3a. It was therefore to link C-1 to C-9a, and the C-3 linked C-3a is reasonable based on chemical shift of the quaternary carbon C-3a (δ 121.6). Since the singlet proton H-5 at δ 7.12 correlated to both C-6 and C-7, it should to be placed in paraposition with respect to H-8. H-5 also correlated to C-4 and C-8a from their weak correlation, and the ROE correlation between H-5 and H-6' confirmed the position of the tetrasubstituted phenyl ring. The last carbon C-9a remained was δ 124.9 compared with that of oleraisoindole (Table S2). As a result, the compound was identified as the 6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxyphenethyl)-7-methoxy-1*H*-benzo[*f*]isoindole-1,3(2*H*)-dione and was given the trivial name oleraisoindole A (Experimental section, in supplementary material).

Among these natural products, alkaloids are considered to be the most promising candidates for use in the treatment of AD, such as physostigmine (eserine) have been long recognized as acetyl- and butyrylcholinesterase (BChE) inhibitors, due to their complex nitrogen-containing structures (Pereira et al. 2010). The inhibition of AChE, the key enzyme in the breakdown of acetylcholine, is currently the main pharmacological strategy available for AD (Konrath et al. 2013). Consequently, the anticholinesterase effect of oleraisoindole A was determined using a microplate assay with the sample of concentrations from 2.5 to 40 μ M, and inhibited 50% of AChE activity (IC₅₀) were presented in Table S3. Figure S14 showed that the anticholinesterase effect of oleraisoindole A was dose-dependent. Anticholinesterase effect was determined according to the modified Ellman method (Ellman et al. 1961). The sample solutions in methanol was diluted into five different concentrations and the AChE solution in buffer of PBS (pH 8.0, containing 0.1 mol/L Na₂HPO₄ and

NaH₂PO₄) were mixed in wells a 96-well microplate. Then incubated for 10 minutes at 37°C and added 5,5-dithiobis-2-nitrobenzoic acid (DTNB) to the buffer. Finally, acetylthiocholine iodide (ATCI) was added and the absorbance was monitored spectrophotometrically at 405 nm. The same concentration of eserine was used as a positive control. Instead of samples, methanol was included in the blank control. Each sample was measured in parallel five times and the percentage of inhibition of AChE was calculated using the following formula (Šinko et al. 2007):

$$\text{Anticholinesterase effect (\%)} = [(A_{\text{blank}} - A_{\text{sample}})/A_{\text{blank}}] \times 100\%$$

where, A_{sample} is the absorbance of the test compound, and A_{blank} is the absorbance of the blank control. The anticholinesterase effect was evaluated by the value of IC₅₀, and values are expressed as the means $\pm$ SD for n = 5.

4. Conclusion

A trace (1 mg) new alkaloid, oleraisoindole A possessing the lignan structure was isolated from the extract of *P. oleracea* of 250 kg, and its structure was complicated that only can be determined by 600 MHz NMR with cryogenic probe. In addition, oleraisoindole A presented anticholinesterase effect with an IC₅₀ value of 60.4 μ M.

Supplementary material

Supporting information can be found in the online version of this article.

Disclosure statement

The authors have no conflicts of interest to disclose.

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References

Awad NE. 1994. Lipid content and antimicrobial activity of phenolic constituents of cultivated *Portulaca oleracea* L. Bull Fac Pharm Cairo Univ. 32:137-142.

Elkhayat ES, Ibrahim SR.M and Aziz MA. 2008. Portulene, a new diterpene from *Portulaca oleracea* L.. J Asian Nat Prod Res. 10:1039-1043.

Erkan N. 2012. Antioxidant activity and phenolic compounds of fractions from *Portulaca oleracea* L. Food Chem. 133:775-781.

Frederich M, Tits M and Angenot L. 2008. Potential antimalarial activity of indole alkaloids. T Roy Soc Trop Med H. 102:11-19.

Howes MJR and Houghton PJ. 2003. Plants used in chinese and indian traditional medicine for improvement of memory and cognitive function. Pharmacol Biochem Be. 75:513-527.

Jiang MY, Zhang WJ, Yang X, Xiu F, Xu HR, Ying XX and Stien D. 2018. An isoindole alkaloid from *Portulaca oleracea* L. Nat Prod Res. 32:2431-2436.

Konrath EL, Passos CDS, Klein-Júnior LC and Henriques AT. 2013. Alkaloids as a source of potential anticholinesterase inhibitors for the treatment of alzheimer's

disease. J Pharm Pharmacol, 65:1701-1725.

Li CY, Ying ZM, Gao MZ, Wei WJ, Hao D, Xu L, Tao XJ, Zhang WJ, Ying XX and Liu J. 2017. Two new similar alkaloids from *Portulaca oleracea* L. Nat Prod Res. 31:1792-1798.

Ma YF, Bao YR, Zhang WJ, Ying XX and Stien D. 2018. Four lignans from *Portulaca oleracea* L. and its antioxidant activities. Nat Prod Res. DOI:10.1080/14786419.2018.1534852.

Meng YH, Ying ZM, Xiang Z, Hao D, Zhang WJ, Zheng Y, Gao YC and Ying XX. 2016. The anti-inflammation and pharmacokinetics of a novel alkaloid from *Portulaca oleracea* L. J Pharm Pharmacol. 68:397-405.

Okafor IA, Ayalokunrin MB and Orachu LA. 2014. A review on *Portulaca oleracea* (Purslane) plant – Its nature and biomedical benefits. International Journal of Biomedical Research. 5:75.

Pereira DM, Ferreres F, Oliveira JMA, Luís Gaspar, Faria J, Patrícia Valentão, Sottomayor M and Andrade PB. 2010. Pharmacological effects of catharanthus roseus root alkaloids in acetylcholinesterase inhibition and cholinergic neurotransmission. Phytomedicine, 17:646-652.

Racková L, Májeková M, Kost'álová D and Štefek M. 2004. Antiradical and antioxidant activities of alkaloids isolated from *Mahonia aquifolium*. Structural

aspects. *Bioorgan Med Chem.* 12:4709-4715.

The Pharmacopoeia Commission of PRC. 2015. THE PHARMACOPOEIA OF THE PEOPLE'S REPUBLIC OF CHINA (Part 1, p.49-50) Beijing. China Medical Science And Technology Press.

Xiu F, Li XT, Zhang WJ, He F, Ying XX and Stien D. 2018. A new alkaloid from *Portulaca oleracea* L. and its antiacetylcholinesterase activity. *Nat Prod Res.* DOI:10.1080/14786419.2018.1460833.

Xu L, Ying ZM, Wei WJ, Hao D, Wang HB, Zhang WJ, Li CY, Jiang MY, Ying XX and Liu J. 2017. A novel alkaloid from *Portulaca oleracea* L. *Nat Prod Res.* 31:902-908.

Yang X, Ying ZM, Liu HR, Ying XX and Yang GL. 2018. A new homoisoflavone from *Portulaca oleracea* L. and its antioxidant activity. *Nat Prod Res.* DOI:10.1080/14786419.2018.1484465.

Yang X, Zhang WJ, Ying XX and Stien D. 2018. New flavonoids from *Portulaca oleracea* L. and their activities. *Fitoterapia.* 127:257-262.

Zhao CC, Ying ZM, Tao XJ, Jiang MY, Ying XX and Yang GL. 2018. A new lactam alkaloid from *Portulaca oleracea* L. and its cytotoxicity. *Nat Prod Res.* 32:1548-1553.