INTRODUCTION

Nicotiana tabacum L, a perennial herbaceous plant, is one of the most commercially valued agricultural crops in the world. The leaves of N. tabacum are the most important raw material for cigarette industry. In addition to being used in cigarette industry, N. tabacum was found to be rich in many useful chemical compounds, such as sesquiterpenes, diterpenoids, alkaloids, lignans, flavonoid, phenylpropanoids and the like. Motivated by search for bioactive metabolites from this plant, an investigation on the chemical constituents of the leaves of oriental tobacco (a variant of N. tabacum L) was carried out. As a result, four types of 2-arylbenzofurans (1-4), including a new compound, tobarylbenzofuran A (1), were isolated from the leaves of oriental tobacco (a variety of Nicotiana tabacum L). Their structures were elucidated by spectroscopic methods, including extensive 1D and 2D NMR techniques. The two compounds were tested for their cytotoxicity against five human tumor (NB4, A549, SHSY5Y, PC3, and MCF7) cell lines. The results showed that compound 1 showed notable inhibitory effect against SHSY5Y and MCF7 cell lines, with IC\textsubscript{50} values of 3.5 and 1.8 µM, respectively.

Key Words: 2-Arylbenzofuran, Oriental tobacco, Cytotoxicity, Nicotiana tabacum L.

EXPERIMENTAL

Four types of 2-arylbenzofurans (1-4), including a new compound, tobarylbenzofuran A (1), were isolated from the leaves of oriental tobacco (a variety of Nicotiana tabacum L). Their structures were elucidated by spectroscopic methods, including extensive 1D and 2D NMR techniques. The two compounds were tested for their cytotoxicity against five human tumor (NB4, A549, SHSY5Y, PC3, and MCF7) cell lines. The results showed that compound 1 showed notable inhibitory effect against SHSY5Y and MCF7 cell lines, with IC\textsubscript{50} values of 3.5 and 1.8 µM, respectively.

Key Words: 2-Arylbenzofuran, Oriental tobacco, Cytotoxicity, Nicotiana tabacum L.
rate 12 mL/min) to give 1 (22.8 mg). On the other hand, separation of fraction C (19.5 g) by silica gel (300-400 mesh) column chromatography, eluted with CHCl₃-(CH₃)₂CO and followed by semi-preparative HPLC (38 % MeOH-H₂O, flow rate 12 mL/min) offered 2 (10.6 mg). Further separation of fraction D (38.8 g) by silica gel (300-400 mesh) column chromatography, eluted with CHCl₃-(CH₃)₂CO and followed by semi-preparative HPLC (28 % MeOH-H₂O, flow rate 12 mL/min) led to the purification of 3 (10.6 mg) and 4 (22.5 mg).

Tobarylbenzofuran A (1): C₁₉H₁₈O₃, orange gum; UV (CH₃OH), λ_
max (log ε) 210 (4.05), 295 (3.86), 345 (3.48) nm; IR (KBr, ν, cm⁻¹): 3340, 2984, 2875, 1603 1538, 1440, 1122, 1061; ¹H and ¹³C NMR data (C₆D₆, N₅00 and 125 MHz) see Table-1; negative ESIMS m/z 291 [M-H]⁻; negative HRESIMS m/z [M-H]⁻ 291.1018. (calcd. (%) for C₁₉H₁₉O₃).

RESULTS AND DISCUSSION

A 70 % aq. methanol extract prepared from the leaves of oriental tobacco was subjected repeatedly to column chromatography on silica gel, sephadex LH-20, RP-18 and preparative HPLC to afford a new 2-arylbenzofuran, tobarylbenzofuran, together with three known 2-arylbenzofurans (1-4). The structures of the compounds 1-4 were as shown in Fig. 1 and the ¹H and ¹³C NMR data of 1 were listed in Table-1. The known compounds, compared with literature, were identified as moracin M (2)¹⁶, moracin M 3'-O-β-D-glucopyranoside (3)¹⁶ and schoenoside (4)¹⁷.

Fig. 1. Structures of arylbenzofurans from oriental tobacco

Compound 1 was obtained as an orange gum. It gave a parent ion by HRMS at m/z 291.1018 [M-H]⁻ (calcd. for 291.1021 corresponding to a molecular formula C₁₉H₁₈O₃).

Strong absorption bands accounting for hydroxy (3340 cm⁻¹) and aromatic groups (1603 1538, 1440 cm⁻¹) could also be observed in its IR spectrum. The UV spectrum of 1 showed absorption maxima at 295 and 345 nm, which confirmed the existence of the aromatic functions. Its ¹H, ¹³C and DEPT NMR spectra (Table-1) showed signals for 19 carbons and 16 hydrogen atoms, corresponding to one 2-arylbenzofuran system (δC(155.2, 105.9, 106.8, 152.7, 113.5, 110.4, 123.2, 150.8, 124.0, 130.2 (2C), 115.8 (2C), 158.2 s) with seven aromatic protons (δH(7.04 s, 1H; 7.96 s, 1H; 7.35 s, 1H; 7.92 d, 1H; 6.62 d, 1H; 5.64 d, 1H; 1.53 s, 4H)).

Table-1; negative ESIMS m/z 291 [M-H]⁻; negative HRESIMS m/z [M-H]⁻ 291.1018. (calcd. (%) for C₁₉H₁₉O₃, 291.1021).

Since certain of the 2-arylbenzofurans exhibit potential cytotoxicity,¹⁸,¹⁹ compounds 1-4 were tested for their cytotoxicities against five human tumor cell lines (NB4, A549, SHS5Y5, PC3 and MCF7) using the MTT method as reported previously.²⁰ Taxol was used as the positive control. The results were shown in Table-2. Compound 1 showed notable inhibitory effect against SHS5Y5 and MCF7 cell lines, with IC₅₀ values of 3.5 and 1.8 µM, respectively.

Table-2; negative ESIMS m/z 291 [M-H]⁻; negative HRESIMS m/z [M-H]⁻ 291.1018. (calcd. (%) for C₁₉H₁₉O₃, 291.1021).
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