SUPPLEMENTARY MATERIAL

Pseudolycorine-\textit{N}-oxide, a new \textit{N}-oxide from \textit{Narcissus tazetta}

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ABSTRACT

A new \textit{N}-oxide, Pseudolycorine \textit{N}-oxide (1) was characterised along with eleven known alkaloids homolycorine (2), \textit{O}-methylmaritidine (3), 8-\textit{O}-demethylhomolycorine (4), homolycorine \textit{N}-oxide (5), lycorine (6), narciclasine (7), pseudolycorine (8), ungeremine (9), 8-\textit{O}-demethylmaritidine (10), zefbetaine (11) and lycorine \textit{N}-oxide (12), from \textit{Narcissus tazetta}. Their structures were established on the basis of spectroscopic data analysis. The extract, fractions and isolated compounds were screened for \textit{in vitro} cytotoxicity against two human cancer cell lines, human cervical cancer (SiHa) and human epidermoid carcinoma (KB) cells. The study demonstrated the cytotoxic potential of extract and its chloroform and \textit{n}-butanol fractions. Further, the results revealed the bioactive potential of narciclasine, pseudolycorine and homolycorine alkaloids.

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Table S1: $^1$H (600 MHz) and $^{13}$C (150 MHz) NMR data for Compound 1 ($\delta$ in ppm) in MeOD-$d_4$ ($J$ in Hz).

Table S2: IC$_{50}$ values of extract, fractions and alkaloids against KB and SiHa cell lines in μM.

Figure S1. The $^1$H-$^1$H COSY (---) and key HMBC correlations (H→C) of compound(1).

Figure S2. Structures of the isolated alkaloids.

Figure S3: Growth inhibition by extract and fractions using SRB assay A. *In vitro* cytotoxicity against KB cell lines and B. *In vitro* cytotoxicity against SiHa cell lines

Figure S4: Growth inhibition by Amaryllidaceae alkaloids using SRB assay A. *In vitro* cytotoxicity against KB cell lines and B. *In vitro* cytotoxicity against SiHa cell lines

Figure S5. HRMS spectra for compound 1

Figure S6. $^1$H NMR spectrum for compound 1 in MeOD-$d_4$

Figure S7. $^1$H NMR spectrum expansion for compound 1 in MeOD-$d_4$

Figure S8. $^{13}$C NMR spectrum for compound 1 in MeOD-$d_4$

Figure S9. Expansion of $^{13}$C NMR spectrum for compound 1 in MeOD-$d_4$

Figure S10. DEPT NMR spectrum for compound 1 in MeOD-$d_4$

Figure S11. Expansion of DEPT NMR spectrum for compound 1 in MeOD-$d_4$

Figure S12. HMQC spectrum for compound 1 in MeOD-$d_4$

Figure S13. Expansion of the HMQC spectrum for compound 1

Figure S14. HMBC spectrum for compound 1 in MeOD-$d_4$

Figure S15. Expansion of the HMBC spectrum for compound 1

Figure S16. Expansion of the HMBC spectrum for compound 1 (continued)

Figure S17. $^1$H-$^1$H COSY spectrum for compound 1 in MeOD-$d_4$

Figure S18. Expansion of $^1$H-$^1$H COSY spectrum for compound 1

Figure S19. Expansion of $^1$H-$^1$H COSY spectrum for compound 1

Figure S20. $^1$H-$^1$H NOESY spectrum for compound 1 in MeOD-$d_4$

Figure S21. Expansion for $^1$H-$^1$H NOESY spectrum for compound 1
Table S1: $^1$H (600 MHz) and $^{13}$C (150 MHz) NMR data for Compound 1 ($\delta$ in ppm) in MeOD-$d_4$ ($J$ in Hz).

| Position | $\delta_H$ (ppm) | $\delta_C$ (ppm) | DEPT |
|----------|------------------|------------------|-------|
| 1        | 4.47, brs        | 71.1             | CH    |
| 2        | 4.04, t ($J = 1.8$) | 72.2             | CH    |
| 3        | 5.63, brs        | 122.6            | CH    |
| 4        | -                | 138.0            | C     |
| 4a       | 3.93, d ($J = 11.4$) | 72.9             | CH    |
| 6a       | 4.44, d ($J = 14.6$) | 68.6             | CH$_2$|
| 6β       | 4.65, d ($J = 14.5$) | -                | C     |
| 6a       | -                | 123.3            | C     |
| 7        | 6.63, s          | 112.0            | CH    |
| 8        | -                | 148.3            | C     |
| 9        | -                | 147.2            | C     |
| 10       | 6.79, s          | 112.5            | CH    |
| 10a      | -                | 127.0            | C     |
| 10b      | 3.21, d*($J = 11.8$) | 35.3             | CH    |
| 11α      | 2.85-2.91, m     | 27.2             | CH$_2$|
| 11β      | 2.68-2.72, m     | -                | C     |
| 12α      | 3.75-3.78, m     | 69.1             | CH$_2$|
| 12β      | 3.64-3.69, m     | -                | C     |

*overlapped signals

Table S2: IC$_{50}$ values of extract, fractions and alkaloids against KB and SiHa cells.

| Extract       | IC$_{50}$ value(µg/mL) |       |       |
|---------------|------------------------|-------|-------|
|               |                        | SiHa  | KB    |
| Extract       |                        | 131.16| >200  |
| Fractions     |                        |       |       |
| $n$-hexane    |                        | >200  | >200  |
| Chloroform    |                        | 85.54 | 88.86 |
| $n$-butanol   |                        | <25   | >200  |
| Water         |                        | >200  | >200  |
| Alkaloids     | IC$_{50}$ value(µM)    |       |       |
| Pseudolycorine $N$-oxide (1) | >100 | >100 |
| Homolycorine (2)          | >100 | <10  |
| $O$-methyl maritidine (3) | >100 | >100 |
| 8-$O$-demethylhomolycorine (4) | >100 | >100 |
| Homolycorine $N$-oxide (5) | >100 | >100 |
| Narcicasine (7)           | <10  | <10  |
| Pseudolycorine (8)        | 124.24 | <10  |
| 8-$O$-demethylmaritidine (10) | 38.4 | >100 |
| Zerbetaine (11)           | >100  | >100 |
| Lycorine $N$-oxide (12)   | >100  | >100 |

SI3
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Figure S2. Structures of the isolated alkaloids (2-12).
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