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REVIEW PAPER

Pyridoacridine alkaloids from deep-water marine organisms: Structural elucidation

Sabrin R.M. Ibrahim [a,b,*], **Gamal A. Mohamed** [c,d]

[a] *Department of Pharmacognosy and Pharmaceutical Chemistry, College of Pharmacy, Taibah University, Al Madinah Al Munawwarah 30078, Saudi Arabia*
[b] *Department of Pharmacognosy, Faculty of Pharmacy, Assiut University, Assiut 71526, Egypt*
[c] *Department of Natural Products and Alternative Medicine, Faculty of Pharmacy, King Abdulaziz University, Jeddah 21589, Saudi Arabia*
[d] *Department of Pharmacognosy, Faculty of Pharmacy, Al-Azhar University, Assiut Branch, Assiut 71524, Egypt*

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KEYWORDS

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Pyridoacridine;
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NMR spectral data

Abstract Pyridoacridine alkaloids are unique marine nitrogenous compounds that represent a large family of alkaloids. They have been reported from different marine organisms like sponges, ascidians, anemones, prosobranch mollusk, and tunicates. Attention to pyridoacridines has risen because of their significant biological activities. The present review emphasizes mainly on pyridoacridines isolated marine organisms over the last years. Thus, the synthetic ones were not discussed. Herein, 95 pyridoacridine alkaloids isolated from marine organisms have been retrieved, in addition to their classification, isolation, sources, structures, molecular weight, physical, and (UV, IR, ^{1}H and ^{13}C NMR) spectral data.

Contents

* Corresponding author at: Department of Pharmacognosy and Pharmaceutical Chemistry, College of Pharmacy, Taibah University, Al Madinah Al Munawwarah 30078, Saudi Arabia. Fax: +966 581183034.
E-mail address: sabrinshaur@gmail.com (S.R.M. Ibrahim).

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1. Introduction

Secondary metabolites from natural sources still provide potential drug candidates with unique skeletons that are interesting for many synthetic approaches. Chemistry researches of marine natural products have yielded great numbers of important metabolites with significant bioactivities. Marine organisms yield various toxic metabolites in order to prevent parasitism and predation as well as to mediate spatial competition.[1,2] Among these toxic metabolites are pyridoacridines. They are the largest group of alkaloids isolated from marine organisms. They have been reported from sponges, ascidians, anemones, tunicates, and prosobranch mollusk, which are decorated with bright colors.[3,4] They have different colors: yellow, deep red, orange, blue, or purple. Their colors were attributed to the presence of pyridoacridines. Pyridoacridines colors change according to the pH. So, they may be used as an indicator. This property is due to the presence of basic nitrogen in the pyridine ring that associated with a chromophore. Generally, pyridoacridines are crystalline compounds with melting points >300 °C. They were isolated as salts of hydrochloric acid. The optical activity of some pyridoacridines is due to the additional asymmetric side chain. They are planar polycyclic heteroaromatic compounds, having 11*H*-pyrido[4,3,2,*mn*]acridine (**1**) or 8*H*-pyrido[4,3,2-*nm*]acridone (**2**) skeletons (Fig. 1), usually possessing different alkylamine side chains

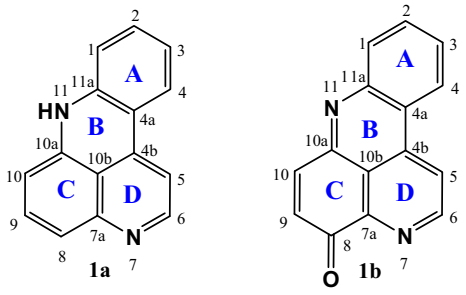
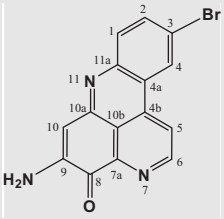


Figure 1 Basic skeletons of pyridoacridine alkaloids.

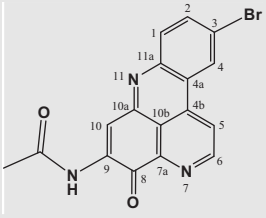
Table 1 Tetracyclic pyridoacridine alkaloids.

Pantherinine (***1***)



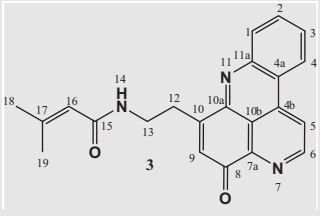
Purple powder; IR (KBr) ν_{max}: 3810 (br), 3720 (br), 1665 (w), 1630 (s) cm^{-1}; UV (MeOH) λ_{max} (ε): 254 (16,110), 316 (3950), 472 (br, 1620) nm; ^1H NMR (DMSO-d_6, 300 MHz): δ_H 7.87 (d, J = 8.7 Hz, H-1), 7.96 (dd, J = 8.8, 1.8 Hz, H-2), 8.99 (d, J = 1.8 Hz, H-4), 8.97 (d, J = 5.5 Hz, H-5), 9.18 (d, J = 5.5 Hz, H-6), 6.58 (s, H-10), 6.60, 8.46 (N*H*); ^1H NMR ($CDCl_3$/CD_3OD, 300 MHz): δ_H 7.82 (d, J = 8.7 Hz, H-1), 7.89 (dd, J = 8.7, 2.1 Hz, H-2), 8.72 (d, J = 2.1 Hz, H-4), 8.69 (d, J = 5.7 Hz, H-5), 9.10 (d, J = 5.7 Hz, H-6), 6.64 (s, H-10); South Australia ascidian *Aplidium pantherinum*[34]

Pantherinine acetate (***2***)



Red glass: UV (MeOH) λ_{max} (ε): 255 (5794), 293 (2811), 432 (1369) nm; IR (KBr) ν_{max}: 3340, 1700 (w), 1655 (s), 1521 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ_H 8.12 (d, J = 8.5 Hz, H-1), 7.98 (dd, J = 8.5, 2.0 Hz, H-2), 8.66 (d, J = 2.0 Hz, H-4), 8.55 (d, J = 5.5 Hz, H-5), 9.29 (d, J = 5.5 Hz, H-6), 8.82 (s, H-10), 8.50 (N*H*), 2.38 (CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 132.21 (C-1), 135.17 (C-2), 122.31 (C-3), 125.91 (C-4), 123.37 (C-4a), 136.01 (C-4b), 120.75 (C-5), 150.03 (C-6), 144.79 (C-7a), 178.32 (C-8), 151.34 (C-9), 121.78 (C-10), 137.06 (C-10a), 116.33 (C-10b), 144.91 (C-10c), 170.38 (Ac); LRMS m/z (%): 369 (25), 367 (24), 327 (96), 325 (100), 300 (63), 298 (67); South Australia ascidian *Aplidium pantherinum*[34]

Cystodytin A (***3***)



Yellow crystals; mp 181–183 °C; UV (MeOH) λ_{max} (ε): 225 (35,000), 272 (25,000), 380 (11,400) nm; IR (KBr) ν_{max}: 3290, 2925, 2850, 1660, 1640, 1590, 1520, 1330, 1300, 1180, 860, 760 cm^{-1}; ^1H NMR ($CDCl_3$/CD_3OD (2:1), 400 MHz): δ_H 8.07 (dd, J = 8.2, 1.4 Hz, H-1), 7.76 (ddd, J = 8.2, 8.1, 1.3 Hz, H-2), 7.64 (ddd, J = 8.1, 8.1, 1.4 Hz, H-3), 8.30 (dd, J = 8.1, 1.3 Hz, H-4), 8.22 (d, J = 5.5 Hz, H-5), 8.81 (d, J = 5.5 Hz, H-6), 3.08 (t, J = 6.4 Hz, H-12), 3.59 (t, J = 6.4 Hz, H-13), 6.01 (brs, H-14), 5.50 (qq, J = 1.4, 1.3 Hz, H-16), 1.65 (d, J = 1.4 Hz, H-18), 1.93 (d, J = 1.3 Hz, H-19); ^{13}C NMR ($CDCl_3$/CD_3OD (2:1), 100 MHz): δ_C 131.6 (C-1), 131.7 (C-2), 129.8 (C-3), 122.8 (C-4), 121.3 (C-4a), 136.9 (C-4b), 119.4 (C-5), 149.0 (C-6), 145.8 (C-7a), 183.2 (C-8), 132.0 (C-9), 152.4 (C-10), 149.8 (C-10a), 117.5 (C-10b), 145.0 (C-11a), 31.3 (C-12), 38.4 (C-13), 167.8 (C-15), 118.1 (C-16), 150.8 (C-17), 26.7 (C-18), 19.4 (C-19); EIMS m/z: 359 $[M+2]^+$, 357 $[M]^+$, 328, 273, 260, 247; HRFABMS m/z: 360.1707 $[M+H+2H]^+$ (calcd for $C_{22}H_{22}O_2N_3$ 360.1712); Okinawan tunicate *Cystodytes dellechiajei*[20]