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STRUCTURE AND DISTRIBUTION OF A NEUROTOXIC PRINCIPLE, HEMEROCALLIN

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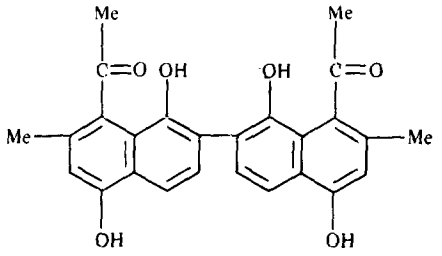
Key Word Index—Hemerocallis; Liliaceae; day lilies; binaphthols, hemerocallin; stypandrol.

Abstract—Hemerocallin, the neurotoxic principle found in *Hemerocallis* species, is the same as stypandrol isolated from *Stypandra imbricata* and *Dianella revoluta*, and the structure ascribed to hemerocallin is incorrect.

INTRODUCTION

The roots of *Hemerocallis* species (day lilies) ingested by goats, sheep and cattle, and used for the treatment of schistosomiasis (snail fever) in humans, have caused fatalities in the People's Republic of China. *H. thunbergii* [1], *H. esculenta* [2], *H. altissima*, *H. lilio-asphodelus* and *H. minor* [3] are toxic. The active principle, originally isolated from the roots of *H. thunbergii* and named hemercallin [4], is reported to have structure **1** [5]. The leaves of *Stypandra imbricata* (blind grass) contain the toxic principle, stypandrol [6], also present in the leaves of *Dianella revoluta* (blue-flax lily) [7], which is believed to have structure **2** [6]. The clinical and pathological effects produced by hemerocallin and stypandrol are reportedly identical [2, 3, 8]. Their ability to induce mydriasis, progressive and irreversible blindness, and paralysis and the nature of the characteristic lesions produced in the nervous system are striking features in all species. These effects appear unlikely to be caused by two chemically different substances.

The present work investigates whether or not hemerocallin and stypandrol are the same material and if the published structures are correct or not.



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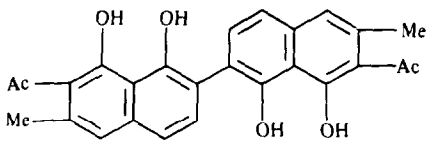

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RESULTS AND DISCUSSION

The results of ^{13}C NMR (DMSO-d_6) examination of hemerocallin: δ204.1, *s*, acetyl carbonyl; 157.0, *s*, C-8–OH; 156.8, *s*, C-1–OH; 135.2, *s*, C-6–Me; 132.8, *s*, C-7–Ac; 130.5, *d*, C-3; 121.4, *s*, C-10; 120.2, *s*, C-2; 117.7, *d*, C-5; 116.3, *d*, C-4; 114.7, *s*, C-9; 32.2, *q*, acetyl Me; 20.2, *q*, aryl Me, are remarkably similar to those published for stypandrol [6]. This is also true of the ^1H NMR (DMSO-d_6) results: δ7.50, 1H, *d*, $J_{3,4}$ 8.58 Hz, H-3; 7.10, 1H, *d*, $J_{4,3}$ 8.58 Hz, H-4; 6.96, 1H, *s*, $W_{h/2}$ 3 Hz, H-5; 2.55, 3H, *s*, acetyl Me; 2.26, 3H, *s*, $W_{h/2}$ 3 Hz, aryl Me. The IR data for hemerocallin: 1615 (*s*), 1570 (*m*), 1405 (*m*), 1315 (*m*), 1088 (*m*), 980 (*m*), 850 (*m*) [3], are comparable with those for stypandrol [6] except that the values for the latter are 0.5%, with a range of +4 to 10 cm^{-1}, higher. The melting points of hemerocallin and its tetra-acetyl derivative (266–269° and 240–241°, respectively) [5] and stypandrol and its tetra-acetyl derivative (265–266° and 241–242°, respectively) [6] are also very similar. Thin layer chromatography of the tetra-acetyl derivatives of hemerocallin and stypandrol showed that they have identical mobility in eight widely different solvent systems. These observations are consistent with hemerocallin and stypandrol being the same material. X-Ray powder photographs of hemerocallin gave patterns comparable with those published for stypandrol [6]. Hemerocallin also produced a volatile (GC) derivative with butaneboronic acid. These findings are in agreement with hemerocallin having structure **2** but not **1**. Our own data and that published lead to the conclusion that (a) hemerocallin and stypandrol are the same; (b) this material has structure **2**; (c) it occurs in *D. revoluta and S. imbricata* as well as *Hemerocallis* species.

EXPERIMENTAL

Preparation of authentic hemerocallin [3]. *H. lilio-asphodelus* roots, collected in Shaanxi province, China, were dried (60°), milled to a fine powder, and extracted with $CHCl_3$. The extract was evapd to dryness under red. pres. (50°) and the residue washed with Et_2O. The washed residue was extracted with Me_2CO saturated with 10% (w/v) aq. NaOH and the extract applied to a neutral Al_2O_3 column prepared in Me_2CO. The column was eluted with alkaline Me_2CO and the yellow hemerocallin-containing band, in the first part of the eluate, collected. This was concd to a small vol. under red. pres. (50°), neutralized with HCl (5%), and the hemerocallin ppt. collected by centrifugation and desiccated over silica gel.

NMR spectroscopic examiniations of hemerocallin. Hemerocallin was dissolved in DMSO-d_6 and its 270 MHz ^1H and 68 MHz ^{13}C NMR spectra determined. The NMR chemical shifts relative to TMS and the solvent for the ^1H and ^{13}C spectra, respectively, were recorded.

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