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Anti-inflammatory flavan alkaloids from the bulbs of *Hymenocallis littoralis* (Jacq.) Salisb

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ABSTRACT

Hymenocallis littoralis (Jacq.) Salisb. (Coastal Spider Lily) is a rich source of structurally diverse specialized metabolites. In the present study, a phytochemical investigation of the bulbs of *H. littoralis* (collected in Guangdong, China) led to the isolation of 12 previously undescribed flavan alkaloids (**1a**/**1b**, **2a**/**2b**, **3a**, **4b**, **5a**/**5b**, **6a**/**6b**, **7**, and **8**). These alkaloids are derived from flavan-pyrrolidinone scaffolds involving multiple stereoisomers. Additionally, two previously undescribed chromones (**12**, **13**), one previously undescribed flavonoid (**9**), and twelve known flavonoids were obtained (**10**, **11**, **14-21**). The structures of the isolates were established through extensive spectroscopic analyses, including HR-ESI-MS, 1D/2D NMR, and ECD calculations. All compounds were evaluated for their anti-inflammatory effects against LPS-induced NO production in RAW 264.7 macrophages. Notably, compounds **2a**, **6a**, and **7** exhibited significant inhibitory activities, with IC_{50} values of 9.95 ± 3.05, 12.36 ± 2.68, and $23.04 \pm 5.19\ \mu M$, respectively. Mechanistic studies indicated that these active compounds suppressed NF-κB activation and downregulated downstream inflammatory mediators. These findings identify *H. littoralis* as a promising source of unique flavan alkaloids and offer a foundation for future structure-activity relationship studies.

1. Introduction

Hymenocallis littoralis (Jacq.) Salisb., commonly known as the Coastal Spider Lily, is a perennial herbaceous plant belonging to the family Amaryllidaceae, native to the coastal regions of Central America, western Florida, and southern Mexico (Zhang et al., 2022). As both a horticultural and medicinal plant, it is well recognized for its rich alkaloid content (Ma et al., 2022). Traditionally, *H. littoralis* has been used in Chinese folk medicine to treat rheumatic joint pain, bruises and swelling, and hemorrhoids. Recent pharmacological studies have revealed that extracts and compounds from *H. littoralis* exhibit cytotoxic activities against several human cancer cell lines, including HepG2, HeLa, SPC-A-1, and FaDu (Le et al., 2023), as well as anti-SARS-CoV-2, anti-inflammatory, and antimicrobial properties (Zhang et al., 2022).

Phytochemical investigations have demonstrated that *H. littoralis* is a rich source of Amaryllidaceae alkaloids, such as pancratistatin, narciclasine, lycorine, haemanthamine, littoraline, and pretazettine (Lin et al., 1995; Pettit et al., 1995). These alkaloids are responsible for many of the plant's notable biological effects and continue to attract attention for their potential in drug discovery and development. However, recent studies have indicated that the non-alkaloid fraction of *H. littoralis* also displays remarkable chemical diversity. Several previously undescribed compounds, including chromones and flavanones, have been isolated from this plant (Anh et al., 2014; Pang et al., 2022). In particular, five previously unreported chromones and one undescribed benzopyran were recently identified with notable anti-inflammatory activities (Guan et al., 2025). These findings not only broaden the known chemical profile of *H. littoralis* but also point to the pharmacological potential of its non-alkaloid constituents. Despite these discoveries, research on the non-alkaloid components of *H. littoralis* is still nascent. Although some previously undescribed compounds have been identified, their pharmacological properties and mechanisms of action have not been fully characterized. This suggests significant untapped therapeutic potential within the plant. Therefore, systematic chemical and biological studies

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Ruyang Guan: Data curation, Formal analysis, Investigation, Writing – original draft. **Meiqi Zhu:** Data curation, Investigation, Methodology. **Mengke Zhang:** Data curation, Formal analysis, Investigation. **Xinyue Liu:** Investigation, Methodology, Validation. **Jinyong Zhang:** Data curation, Formal analysis, Investigation. **Jinghui Wu:** Data curation, Formal analysis, Software. **Jingwen Xu:** Conceptualization, Methodology, Project administration, Writing – review & editing. **Xiangjiu He:** Conceptualization, Funding acquisition, Supervision, Writing – review & editing. **Yihai Wang:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.phytochem.2026.114967.

Data availability

Data will be made available on request.

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