



# Genomic and phylogenetic analyses of the domoic acid biosynthesis genes in the benthic diatom *Nitzschia navis-varingica* (Bacillariophyceae)

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## ARTICLE INFO

### Keywords:

Domoic acid  
Harmful algal bloom  
Neurotoxin  
*Nitzschia navis-varingica*  
*Pseudo-nitzschia*  
Toxin biosynthesis genes  
Comparative genomics

## ABSTRACT

Through genome sequencing and comparative genomic analysis, candidate genes involved in the biosynthesis of domoic acid (DA) in the benthic diatom *Nitzschia navis-varingica* were identified. Orthologs of DA biosynthesis genes (*dabA*, *dabB*, *dabC*, and *dabD*), originally identified in *Pseudo-nitzschia* species, were detected in *N. navis-varingica* strains. However, due to the draft level of our genomes, the tandem gene cluster organization present in the *Pseudo-nitzschia* species cannot be determined in *N. navis-varingica* strains. In addition, two copies of *dabC* were found in *N. navis-varingica* strains, suggesting potential functional significance in the biosynthesis of DA and its isoforms. The identification of *dab* genes in *N. navis-varingica* provides a foundation for further studies on the origin, evolution, and transcriptional regulations of DA biosynthesis in this benthic diatom.

## 1. Introduction

Domoic acid (DA) was first isolated from the red alga *Chondria armata*, where it was found to exhibit notable anthelmintic properties (Takemoto et al., 1958). The neurotoxin was later identified in the contaminated mussels as the causative agent of amnesic shellfish poisoning (ASP) following a 1987 incident in Prince Edward Island, Canada, where the contaminated mussels caused the deaths of three individuals and illness of over a hundred more (Bates et al., 1989). The planktonic pennate diatom *Pseudo-nitzschia multiseries* was later identified as the producer of DA in this event (Bates et al., 1998). Since then, 62 *Pseudo-nitzschia* species have been identified and currently accepted by AlgaeBase (Guiry and Guiry, 2021), in which nearly one-half have been found to be capable of synthesizing DA (Bates et al., 2018).

In addition to *Pseudo-nitzschia* species, two species of the benthic pennate diatoms, *Nitzschia navis-varingica* and *Nitzschia bizertensis*, have been found to be capable of producing DA (Kotaki et al., 2000; Lundholm and Moestrup, 2000; Bouchouicha Smida et al., 2014). *N. navis-varingica* has garnered significant attention due to its

widespread distribution in the Western Pacific (Puilingi et al., 2022; Tan et al., 2025), primarily inhabiting the benthic habitats of mangrove environments (Tan et al., 2016). Originally discovered in shrimp-culture ponds in Do Son, Vietnam, DA production in *N. navis-varingica* has been well-documented, with the DA content per cell (Kotaki et al. 2000, 2004, 2005, 2008; Bajarias et al. 2006; Romero et al. 2011, 2012; Thoha et al. 2012; Tan et al. 2016; Puilingi et al., 2022) comparable to those of toxigenic *Pseudo-nitzschia* species (Bates et al., 2018). Unlike *Pseudo-nitzschia* species, which predominantly produces DA (Bates et al., 2018), higher proportions of the DA isoforms, isodomoic A (IA) and isodomoic B (IB), were characterized in *N. navis-varingica* (Kotaki et al., 2000), with numerous strains producing IA and/or IB as major components (Kotaki et al., 2006; Tan et al., 2016; Romero et al., 2011; Puilingi et al., 2022). Although a degree of variation in the DA profiles of these strains have been noted (Tan et al., 2016; Puilingi et al., 2022), no clear genotypic differentiation with respect to geographical origins was identified (Tan et al., 2025). These indicate possible intraspecific variations in the DA biosynthesis of this species, suggesting potential varying mechanisms for the differential production of IA and IB.

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<https://doi.org/10.1016/j.hal.2025.102905>

Received 13 February 2025; Received in revised form 13 May 2025; Accepted 25 May 2025

Available online 26 May 2025

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