INTRODUCTION

Albicidin is a potent inhibitor of bacterial DNA gyrase with IC₅₀ values in a nM range, produced by the sugarcane pathogenic bacterium Xanthomonas abalineae [1]. The structure of albicidin remained unclear for more than three decades after its first description by Birch et al. [2]. After the identification and sequencing of three gene islands, responsible for the albicidin biosynthesis, a PKS-NRPS hybrid, build up by three enzymes, Alb01, Alb05 and Alb09 was proposed for the albicidin assembly [3, 4]. Most recently we were able to solve the hitherto unknown structure, revealing a unique polyaromatic oligopeptide mainly composed of p-amino benzoic acids [5, 6]. In vitro studies of the non-ribosomal albicidin assembly line provided further insights into the biosynthetic machinery of albicidin. Together with our bioinformatic investigations we were able to propose a comprehensive biochemical assembly, expanding the non-ribosomal code of adenylation domains with p-amino benzoic acid derivatives. Furthermore our study reveals a new type of dehydratase domain responsible for the in situ formation and incorporation of cyano-alanine [6].

RESULTS AND DISCUSSION

![Figure 1. The structure of the albicidin. Albicidin is composed of a methylated derivative of p-coumaric acid (MCA), the non-proteinogenic δ-amino acid cyanoalanine (Cya) as well as the aromatic δ-amino acids methylated derivative of p-coumaric acid (MCA), the non-proteinogenic α-amino acids pABA and pMBA.](image1)

**Figure 4. Model of albicidin biosynthesis.** (a) Proposed biosynthetic assembly line for albicidin. Substrates of the NRPS are indicated at the A domains. PKS and NRPS modules are color-coded in blue and green, respectively. (b) Suggested pathways for the biosynthesis of the MCA-1 precursor pMBA-CoA as well as the δ-amino acid cyanoalanine (Cya) as well as the aromatic δ-amino acids methylated derivative of p-coumaric acid (MCA), the non-proteinogenic α-amino acids pABA and pMBA. (c) Suggested mechanism for the transformation of activated Asn into Cya by Alb04. Conventional activation of Asn by adenylation is shown to activate p-aminobenzoic acid derivatives (highlighted in red). However, a new aspartic acid appears for all A domains that have been shown to activate p-aminobenzoic acid derivatives (highlighted in red). Relevant interactions in the substrate binding pockets of A domains are shown for (b) the Phe-activating GrsA (PDB 1amuc) and (c) the structural model of NRPS-1 (based on homology modeling with the ITASER webtool using GrsA as template).

![Figure 5. Substrate specificities of NRPS activation domains in albicidin NRPS modules.](image2)

**Figure 2. Gene cluster of albicidin biosynthesis.**

**REFERENCES**


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