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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐ A description of all covariates tested
☒	☐ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	NCBI-genome-download tool was used to download all "complete", "chromosome", scaffold" and "contig" assembly levels of bacterial genomes from NCBI refseq database. 11 characterized mycosamine related glycosyltransferase were acquired from Genebank. Compound purification was conducted using LCMS (Waters) and HPLC (SHIMADZU,LC-20AT/CBM-20A), Scanning electron microscopy (SEM) was performed with a Hitachi su8010; UV-vis was carried out using Thermo scientific Multiskan SkyHigh enzyme labeler; HRMS analysis was analyzed using Waters-Gs-XS-QTOF and Thermo scientific Q Exactive Orbitrap; ITC experiments were determined using an PEAQ-ITC; the NMR data were analyzed using Bruker AVANCE NEO 600MHz and Bruker AVANCE III HD 700MHz; Mouse muscle and kidney homogenates were prepared using Mettini gentleMACS Automatic Tissue Processor, and Kidney damage biomarker quantifications were performed using Applied Biosystems QuantStudio 3
Data analysis	AntiSMASH 7.0 was used to identify and annotate the biosynthetic gene clusters. MEGA11 was utilized to align multiple amino acids sequences. Online iTOL5.0 was used to visulize the phylogenetic tree. Prism9.0 was used to plot the data curve. Snapgene 6.0.2 software was used for gene konckout.Data and statistics were analyzed using Microsoft excel for Windows (version 10) and Graphpad Prism 9, version 9.5.1 and Origin 2021 (9.8) on the Windows operating system. Chemical structures were drawn using chemdraw 20.0. NMR data was analyzed using MestReNova 14.2.1 . Imagel v1.53a was used for histopathology image processing.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Accession numbers for Known Polyene antibiotics BGCs appear in the Supplementary Table S1.NMR spectra for mandimycin and mandimycin B are presented as Supplementary Information. The raw data of Figure 2, 3, 4 and Extended Figure 3, 5, 7, 8, 9, 10, 11 can be found in the source data file for this manuscript.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	N/A
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	N/A

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	For animal studies sample size was chosen based on experience with the models used to enable identification of differences between treatment and control groups. The numbers of mice numbers were specified in the methods sections and figure legends. In the thigh infection model, each group consisted of 4 mice and 8 thighs. In the nephrotoxicity study, each group included 4 mice. In the disseminated candidiasis model, each group contained 4 mice. In the invasive candidiasis model, each group contained 6 mice. In the skin infection model, each group contained 4 mice. In the vaginitis model, each group contained 4 mice. In the pharmacokinetics study, each group contained 3 rats.
Data exclusions	No data exclusions in this study.
Replication	All experiments were performed in three independent times with reproducible results. MIC were tested in duplicate and repeated in three independent times. The burden of mice infection was calculated using 4 mice in each group, with 2 thighs for each mice.
Randomization	Mice were randomly allocated to treatment groups on arrival.
Blinding	CFU counting in thigh infection model was blinded. Histopathological changes in kidney section were monitored in a blinded fashion. Other experiments not mentioned here were not conducted in a blinded fashion, as the data were analyzed by machine and were not influenced by different operators.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	HepG2, SK-Hep1 cells used in this study was acquired from National Collection of Authenticated Cell Cultures under number of 259876. HK-2 and RPTEC cells were ordered from ATCC under number of CRL1469 and PCS-400-010. The PANC-1 cells were ordered from Shanghai Fuheng Biotechnology Co., Ltd under number of FH0286.
Authentication	The National Collection of Authenticated Cell Cultures (NCACC) was responsible for authenticating the cell line used in the current study. All cell lines were verify using STR profiling.
Mycoplasma contamination	Cell line used in current study was tested negative for mycoplasma contamination by the collection agency.
Commonly misidentified lines (See ICLAC register)	no misidentified lines were found in this study.

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals	Male Sprague-Dawley rats (7 to 8 weeks old) were used for pharmacokinetic studies,Female ICR mice (6 week old) mice were used all infection model. Female ICR mice (6 week old) mice were used in the nephrotoxicity assay.
Wild animals	N/A
Reporting on sex	N/A
Field-collected samples	N/A
Ethics oversight	Ethics statements were included into the methods section.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*