## **Supporting Information**

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# Cyclic Polyketides with α-Glucosidase Inhibitory Activity from *Endiandra kingiana* Gamble and Molecular Docking Study

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Figure S1: Separation and isolation scheme for compound 1-4



Figure S2: HRESIMS spectrum for compound 1



Figure S3: <sup>1</sup>H NMR spectrum for compound 1



Figure S4: <sup>13</sup>C NMR and DEPT-135 spectrum for compound 1



Figure S5: COSY-2D NMR spectrum for compound 1



Figure S6: COSY-2D NMR (expanded) spectrum for compound 1



Figure S7: HMBC-2D NMR spectrum for compound 1





Figure S8: HRESIMS spectrum for compound 2



Figure S9: <sup>1</sup>H NMR spectrum for compound 2



Figure S10: <sup>13</sup>C NMR and DEPT-135 spectrum for compound 2



Figure S11: HRESIMS spectrum for compound 3



Figure S12: <sup>1</sup>H NMR spectrum for compound 3



Figure S13: <sup>13</sup>C NMR spectrum for compound 3





Figure S14: COSY-2D NMR spectrum for compound 3



Figure S15: COSY-2D NMR (expended) spectrum for compound 3



Figure S16: HMBC-2D NMR spectrum for compound 3



Figure S17: HRESIMS spectrum for compound 4



Figure S18: <sup>1</sup>H NMR spectrum for compound 4



Figure S19: <sup>13</sup>C NMR spectrum for compound 4



### **S1**: *Preparation of stock solution:*

Briefly, the phosphate saline buffer was prepared with 50 mM with pH 6.8. Then, 4.214 mg of substrate solution (4-Nitrophenyl  $\alpha$ -D-glucopyranoside) was prepared in 2500 $\mu$ l of phosphate buffer to the final concentration of 0.7 mM. Then, 0.022 mg of the enzyme ( $\alpha$ -glucosidase from *Saccharomyces cerevisiae*) was dissolved in 2000  $\mu$ l of the buffer which contains 0.04 u /well. To make 1 mM solution of inhibitor, 0.641 mg of Acarbose was dissolved in 75  $\mu$ l of 70 % DMSO. In this experiment, 70% DMSO was used for control and to dissolve the test compounds

### **S2:** *α*-glucosidase enzyme inhibition activity:

An *in vitro* antidiabetic activity for tsangibeilin B (2), kingianin A (3), and kingianin F (4) were measured using  $\alpha$ -glucosidase inhibition assay on 96-well microtite plates using  $\alpha$ -glucosidase from *Saccharomyces cerevisiae*. 135 µL of 50 mM phosphate saline buffer with pH 6.8 was dispended into the 96-well plates. Then, 20µL of the test sample in 70% DMSO and 20µl of the enzyme were added into the wells. The reaction mixture was incubated at 37.5 °C for 15 minutes. After the incubation period, a pre-read of the plate was taken by the spectra max. Next, 25µl of the substrate (pNPG) was added and the reading was taken on spectra max at 400 nm for 30 minutes. In the end normal read is taken and the percent inhibition was calculated.

Percentage of inhibition (%) = 
$$\left(\frac{Abs_{control} - Abs_{extract}}{Abs_{control}}\right) \times 100$$

Table S1: Binding interactions details of compound 2-4 docked into N-terminal and C-
terminal of human MGAM

Protein	Compounds	Free energy of binding	Protein Residue	Type of interaction
			TYR299	π-π T-shaped π-alkyl
NtMGAM	2	-5.39	TRP441 TRP539 PHE575 HIS600	π-sigma π-alkyl π-alkyl π-alkyl π-π T-shaped
			GLN603 TYR605	π-alkyl H-bond H-bond

3     -7.50     H-bond ASN207 PHE544 ALA576 TYR605     H-bond alkyl H-bond carbon π-π T-shaped       4     -6.80     MET444 ASP542     Alkof H-bond       4     -6.80     MET444 ALA576     alkyl H-bond       4     -6.80     MET444 ASP542     Alkof H-bond       4     -6.80     MET444 ASP542     alkyl H-bond       4     -6.80     MET444 ASP542     alkyl H-bond       4     -6.80     MET444 ASP542     alkyl H-bond       4     -6.80     TRF605     H-bond       4     -6.80     TRF547     H-bond       4     ASP548     H-bond     H-bond       4     ASP548     H-bond     Attractive charge       Acarbose     -3.23     TRP547     H-bond       4     ASP548     H-bond     Attractive charge       4     -7.11     LYS1460     H-bond       4     -10.87     TRP1369     π-alkyl       7     -10.87     TRP1350     π-alkyl       4     -10.48     TRP1350     π-alkyl					II have d
3     -7.50     ASN207 LEU473 PHE544 ALA576 TYR605     H-bond n-alkyl H-bond carbon n-π T-shaped       4     -6.80     MET444 ALA576 TYR605     alkyl H-bond       4     -6.80     MET444 ALS776     alkyl m-alkyl TYR605       1     ASN207     H-bond       4     -6.80     ALS776     m-alkyl m-alkyl TYR605       1     ASN207     H-bond       1     ASN207     H-bond       1     TYR605     H-bond       1     ASN207     H-bond       1     H-bond     alkyl       1     TYR605     H-bond       1     ASN207     H-bond       1     H-bond     alkyl       1     H-bond     Alfasts       1     H-bond       1     H-bond				<b>THR205</b>	H-bond
3         -7.50         LEU473 PHE544 ALA576 TYR605         H-bond π-πlkyl H-bond carbon π-π T-shaped           4         -6.80         MET444 ASP542         alkyl H-bond           4         -6.80         MET444 ALA576         alkyl π-alkyl LEU577           7         -6.80         MET444 ASP542         alkyl H-bond           4         -6.80         -6.80         MET444 ASP542         alkyl H-bond           4         -6.80         MET444 ASP542         H-bond           4         -6.80         TYR605         H-bond           4         -6.80         TYR605         H-bond           4         -6.80         TYR605         H-bond           4         -6.80         TRP547         H-bond           4         -3.23         TRP547         H-bond           4         -3.23         TRP547         H-bond           4         -3.23         TRP547         H-bond           4         -7.11         TRP1369         π-alkyl           9         Attractive charge         Attractive charge           4         -10.87         TRP1369         π-alkyl           1         TYS1460         H-bond         H-bond           1 <t< td=""><td></td><td rowspan="2"></td><td>ASN207</td><td>H-bond</td></t<>				ASN207	H-bond
3         -7.50         PHE544 ALA576 TYR605         H-bond π-alkyl H-bond carbon π-π T-shaped           4         -6.80         MET444 ALA576         alkyl met144         alkyl ASP542           4         -6.80         MET444 ALA576         alkyl met144         alkyl met144           4         -6.80         MET444         alkyl ASP542         H-bond           4         -6.80         MET444         alkyl ASP542         H-bond           4         -6.80         ALA576         π-alkyl H-bond         alkyl ALA576           4         -6.80         ALA576         m-alkyl H-bond         alkyl H-bond           ASP549         H-bond         H-bond         ALA545           H-bond carbon         H-bond carbon         H-bond carbon           H-bond carbon         H-bond         Attractive charge           ASP548         H-bond         Attractive charge           ASP548         H-bond         Attractive charge           ASP549         Salt bridge         Attractive charge           ASP1526         m-aikyl         H-bond           ASP1520         m-aikyl         H-bond           ASP1520         m-aikyl         H-bond           ASP140         m-aikyl         H-bond		2		LEU473	alkyl
CtMGAM         3         -10.87         TRP1369 $\pi$ -alkyl           4         -6.80         MET444         alkyl           ALA576         T-alkyl         alkyl           ASP542         H-bond         alkyl           ALA576         T-alkyl         alkyl           ALA576         H-bond         H-bond           ALA576         H-bond         TRP647           H-bond carbon         H-bond carbon         H-bond carbon           ALA545         H-bond         H-bond           ALA545         H-bond         alkyl           H-bond carbon         ASP548         H-bond           H-bond carbon         ASP548         H-bond           Asp548         H-bond         Attractive charge           TRP1369 $\pi$ -alkyl         Hebond           Asp1526 $\pi$ -ainion         Hebond           PHE1550 $\pi$ -alkyl         Hebond		3	-7.50	PHE544	H-bond
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CtMGAM		4	-0.80	LEU577	π-alkyl
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$\mathbf{CtMGAM} = \begin{array}{cccc} & & & & & & & & & & & \\ & & & & & & & $					Attractive charge
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$\begin{array}{c ccccccccccccccccccccccccccccccccccc$				PHE1427	$\pi$ -alkyl
$\begin{tabular}{ c c c c c c c c c c } \hline ASP1526 & $$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$$		2	-7.11	LYS1460	H-bond
$\mathbf{CtMGAM} = \begin{array}{c} 3 \\ 4 \end{array} \begin{array}{c} -10.87 \end{array} \\ \begin{array}{c} PHE1560 \\ PRO1159 \\ LYS1164 \\ H-bond \\ ASP1420 \\ T-anion \\ LYS1460 \\ PHE1560 \\ \pi-alkyl \\ THR1586 \\ H-bond \\ TRP1355 \\ \pi-\pi \ stacked \\ TRP1369 \\ \pi-alkyl \\ RG1377 \\ H-bond \\ MET1421 \\ \pi-sulfur \\ LYS1460 \\ H \ barrd \end{array}$				ASP1526	$\pi$ -anion
Relation of the large $1$ and $1$ CtMGAM3-10.87PRO1159 LYS1164alkyl H-bond PHE1560A SP1420 PHE1560 THR1586H-anion LYS1460H-bondPRO1159 alkyl ASP1420 PHE100A SP1420 				PHE1560	π-alkvl
CtMGAM3-10.87LYS1164H-bond ASP1420 $4$ -10.87 $1000000000000000000000000000000000000$	-	3	-10.87	PRO1159	alkyl
CtMGAM3 $-10.87$ ASP1420 LYS1460 PHE1560 TRP1355 $\pi$ -anion $\pi$ -alkyl THR1586 TRP13554 $-10.48$ TRP1355 $\pi$ - $\pi$ stacked TRP1369 ARG1377 MET1421 TH-bond MET1421 TRS1460 H band	CtMGAM			I VS1164	H-bond
CtMGAM       3       -10.87 $\pi$ HSF 1420 $\pi$ -alloit         LYS1460       H-bond         PHE1560 $\pi$ -alkyl         THR1586       H-bond         4       -10.48         4       -10.48 $\pi$ -alkyl         ARG1377         H-bond         MET1421 $\pi$ -sulfur         LYS1460       H-bond				ΔSP1//20	$\pi_{-anion}$
$4 -10.48$ $ETS1400 Heodd PHE1560 \pi-alkylTHR1586 H-bondTRP1355 \pi-\pi stackedTRP1369 \pi-\pi T-shaped\pi-alkylARG1377 H-bondMET1421 \pi-sulfurLYS1460 H hand$				I VS1460	H-bond
$4 -10.48 \begin{array}{c} THE1500 & \pi\text{-arkyr} \\ THR1586 & H\text{-bond} \\ \hline TRP1355 & \pi-\pi \text{ stacked} \\ TRP1369 & \pi-\pi \text{ T-shaped} \\ \pi\text{-alkyl} \\ ARG1377 & H\text{-bond} \\ MET1421 & \pi\text{-sulfur} \\ I XS1460 & H hand \\ \hline \end{array}$				PHE1560	m-ollarl
$4 -10.48 \begin{array}{c} \text{TRP1355} & \pi - \pi \text{ stacked} \\ & \text{TRP1369} & \pi - \pi \text{ T-shaped} \\ & \pi - alkyl \\ \text{ARG1377} & \text{H-bond} \\ & \text{MET1421} & \pi - sulfur \\ & \text{LXS1460} & \text{H b and} \end{array}$				THP1586	h-aikyi U hond
$4 -10.48 \qquad \begin{array}{c} \text{TRP1355} & \pi - \pi \text{ stacked} \\ \text{TRP1369} & \pi - \pi \text{ T-shaped} \\ \pi - alkyl \\ \text{ARG1377} & \text{H-bond} \\ \text{MET1421} & \pi - sulfur \\ \text{LXS1460} & \text{H-bond} \\ \end{array}$				TIR1380	n-bolld
$4 -10.48 \qquad \begin{array}{c} \text{TRP1369} & \pi - \pi \text{ T-shaped} \\ \pi - \text{alkyl} \\ \text{ARG1377} & \text{H-bond} \\ \text{MET1421} & \pi - \text{sulfur} \\ \text{LXS1460} & \text{H-bond} \\ \end{array}$				TKP1355	$\pi$ - $\pi$ stacked
4 -10.48 $\pi$ -alkyl ARG1377 H-bond MET1421 $\pi$ -sulfur LXS1460 H bond				TRP1369	$\pi$ - $\pi$ T-shaped
ARG1377 H-bond MET1421 π-sulfur LVS1460 H bond					π-alkyl
$\begin{array}{ccc} \text{MET1421} & \pi \text{-sulfur} \\ \text{LVS1460} & \text{II b and} \end{array}$				ARG1377	H-bond
IVS1460 II hand				MET1421	$\pi$ -sulfur
LISI400 H-DONU				LYS1460	H-bond

			ASP1526	$\pi$ -anion
			PHE1560	π-alkyl
			GLY1588	Unfavorable donor-
				donor
			ASP1157	H-bond
			GLN1158	H-bond
				H-bond carbon
			LYS1164	H-bond
			ASP1279	H-bond carbon
	A comb coc	10.17		H-bond
	Acarbose	-10.17	ASP1420	Attractive charge
			GLU1451	H-bond
			LYS1460	H-bond
			ARG1510	H-bond
			ASP1526	Salt bridge
			HIS1584	H-bond

## **S3:** *Molecular docking*:

The docking process using AutoDockTool 1.5.6 and Autodock 4.2 involved four steps: the preparation of reference structures (receptors and inhibitor), the preparation of ligands structures (compounds), docking and scoring, and visualization. The reference structures used were N-terminal of human Maltase-Glucoamylase (MGAM) complexed with acarbose (PDB ID: 2QMJ) and C-terminal of human Maltase-Glucoamylase (MGAM) complexed with acarbose (PDB ID: 3TOP), which downloaded from the RCSB PDB website. Briefly, both crystal PDBs were processed using UCSF Chimera software [12], starting by removing water molecules and unrelated heteroatom, followed by the separation of receptor and inhibitor from the complexes into individual structures and finally minimization of individual structures by steepest descent steps. Then, the minimized receptors and inhibitor were saved as PDB formats. The structures of all compounds were built using ChemDraw [13] and subsequently converted from cdx format to PDB.

Simulations of ligand-receptor docking were carried out using Autodock 4.2 software run with a Lamarckian genetic algorithm (LGA) search method [14-15]. AutoDockTools 1.5.6 was used for the generation of input files (rec.pdbqt and lig.pdbqt), the set-up of grid parameter file (rec.gpf) and the production of docking parameter file (lig.dpf). The active site of N-terminal and C-terminal of MGAM were enclosed in the center of the grid box having the size of -29.937, -6.184, -5.476 and -31.713, 35.676, 26.262 points in x, y, z direction respectively, which were the center points for the control (acarbose) binding sites in N-terminal and C-terminal of MGAM. Autogrid4 was executed to generate grid maps log file (rec.glg) for use with Autodock4. During docking, the receptors (N-terminal and C-terminal of MGAM) were set as rigid and the ligands (inhibitor and compounds) were set as flexible. The number of docking runs per simulation was 100 and the output of ligand poses, the docked coordinates, cluster sizes and free energy of binding were generated in the docking log file (lig.dlg). Visual inspection of poses and MGAM-ligands interactions were analyzed using Biovia Discovery Studio Visualizer Client 2020 (Dassault Systèmes BIOVIA, Discovery Studio Modeling Environment, Release 2017, San Diego: Dassault Systèmes, 2016).







