*Article*

# Synthesis, Antimicrobial, Anticancer, PASS, Molecular Docking, Molecular Dynamic Simulations & Pharmacokinetic Predictions of some Methyl β-D-Galactopyranoside Analogs

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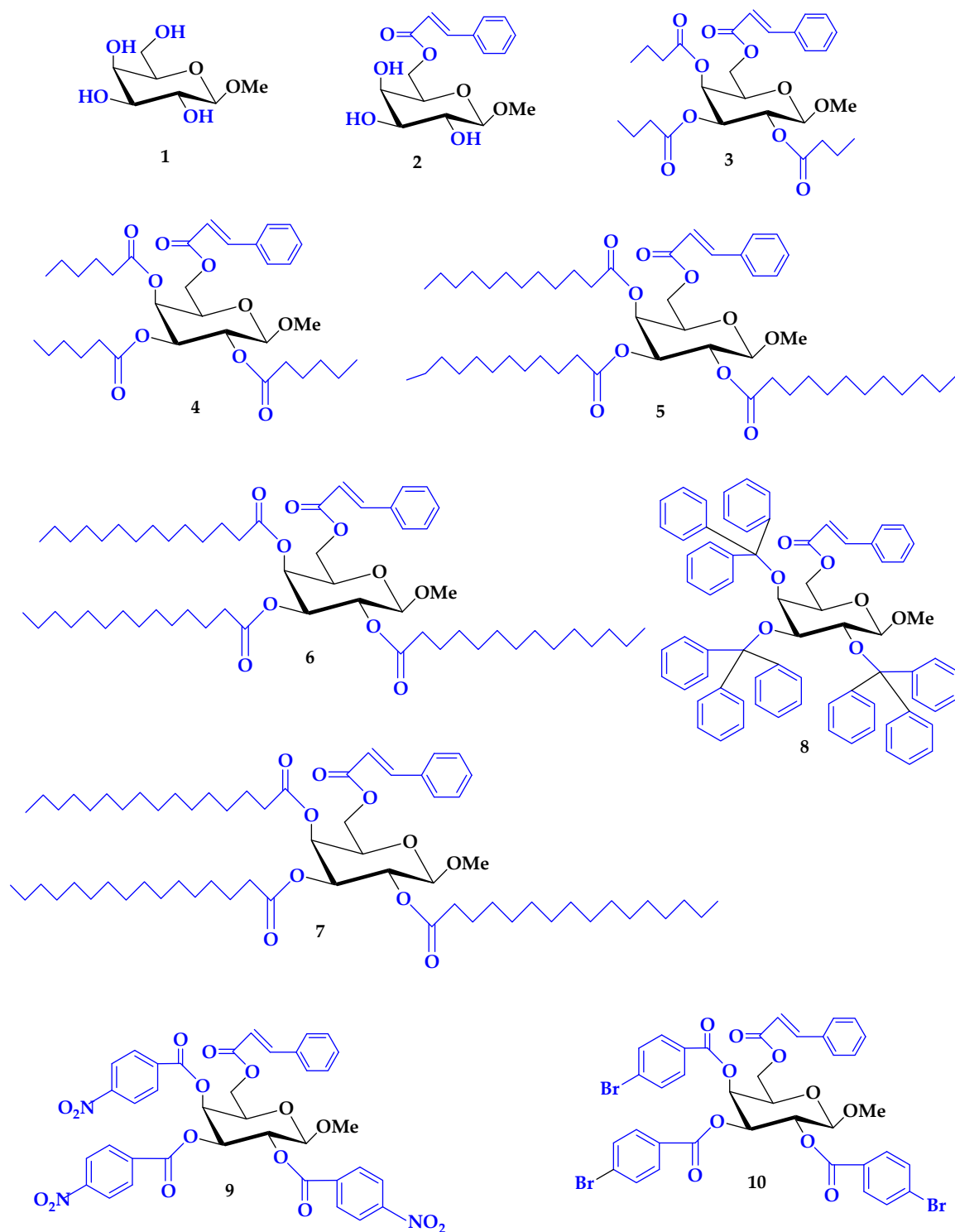* Correspondence: akawsarabe@yahoo.com (SMAK); ozeki@yokohama-cu.ac.jp (YO.)

**Supplementary Materials**

**Figure S1.** 2D structure of designed MGP derivatives (**2-10**).
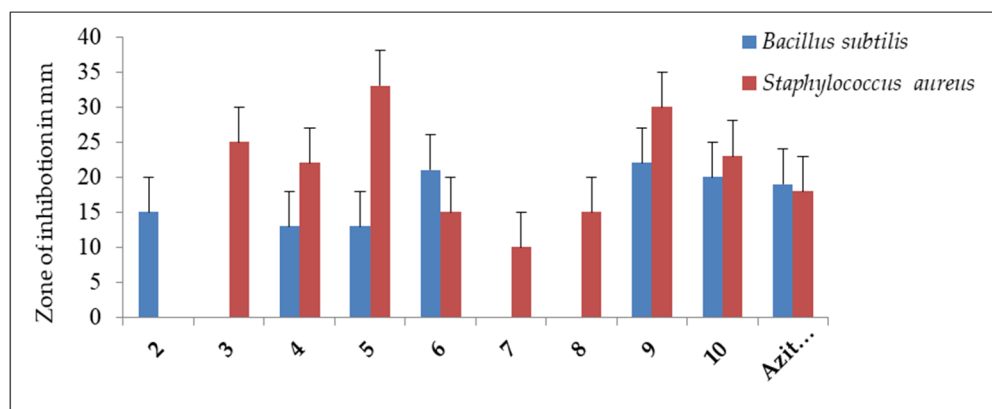
**Figure S2.** Zone of inhibition was observed against Gram-positive bacteria by the tested analogs.
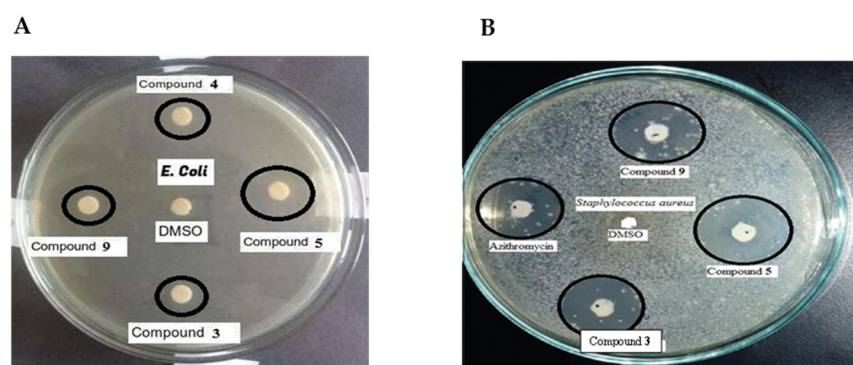
**Figure S3.** Some experimental dishes of the synthesized test analogs against bacteria. **A** against *E. coli* by four test analogs **3, 4, 5,** and **9; B.** against *S. aureus* by test analogs **5, 9,** and **3.** Here DMSO = negative control and Azithromycin = positive control.
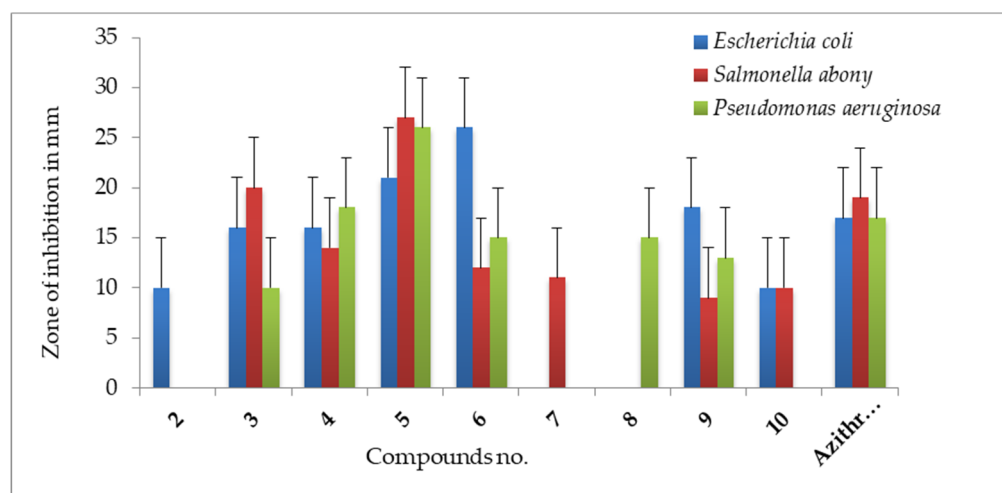
**Figure S4.** Zone of inhibition observed against Gram-negative bacteria by the tested analogs.
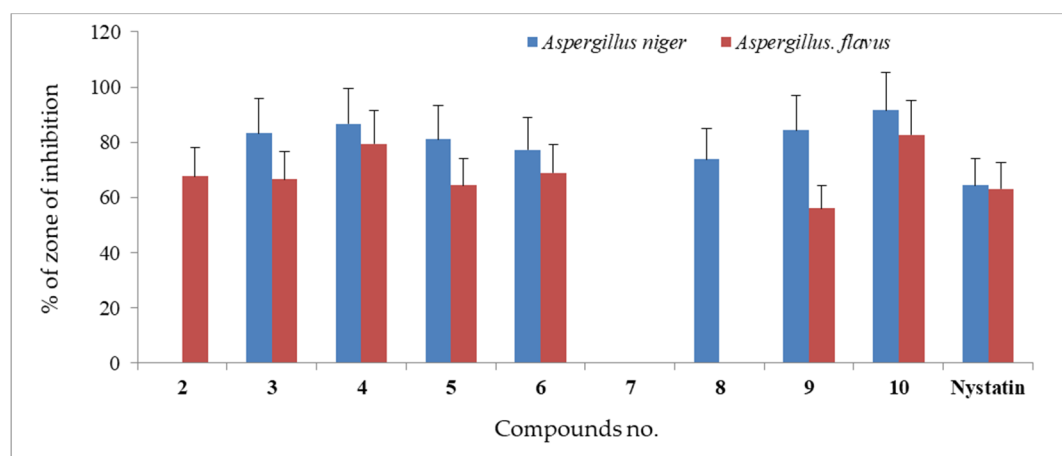
**Figure S5.** Antifungal activities of the synthesized test analogs.
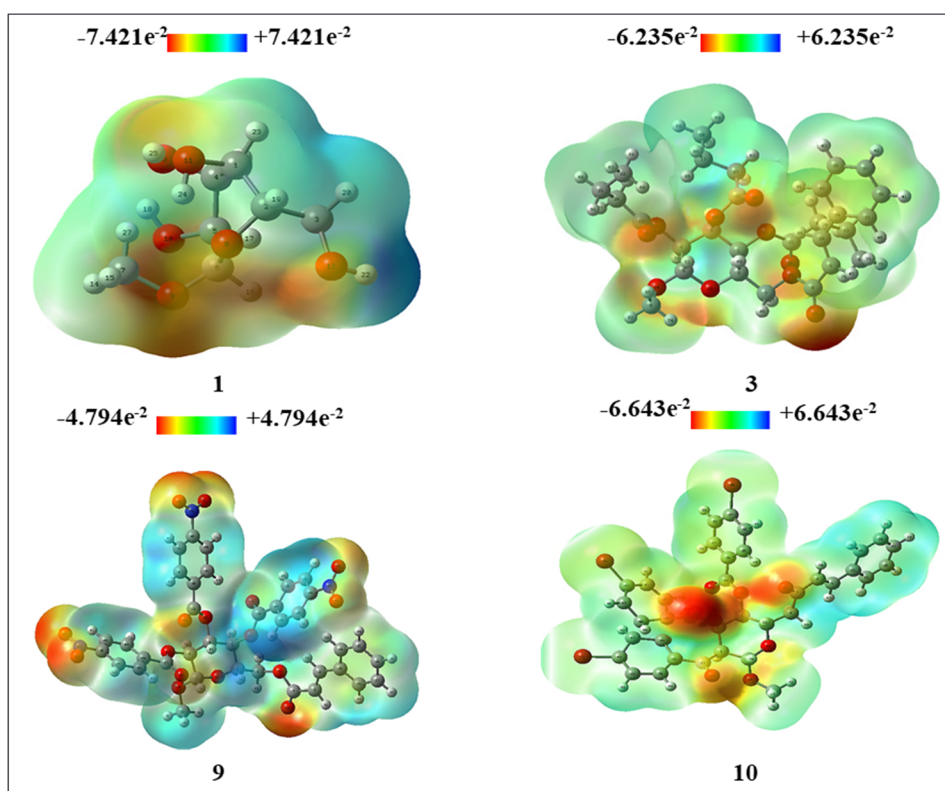
**Figure S6.** Map of the molecular electrostatic potential of MGP (**1**) and analogs (**3, 9,** and **10**).
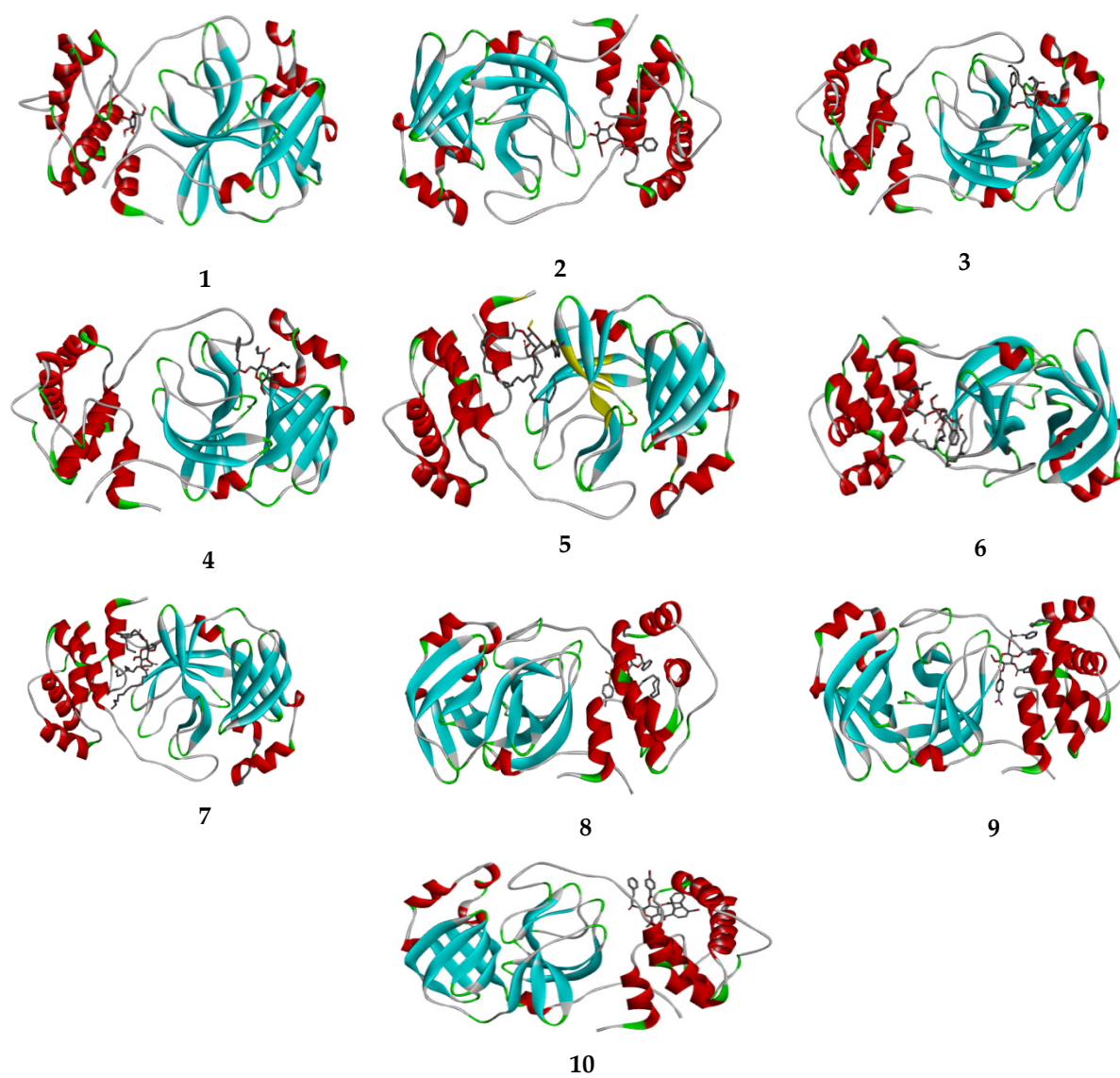
**Figure S7.** Docked view of all compounds.
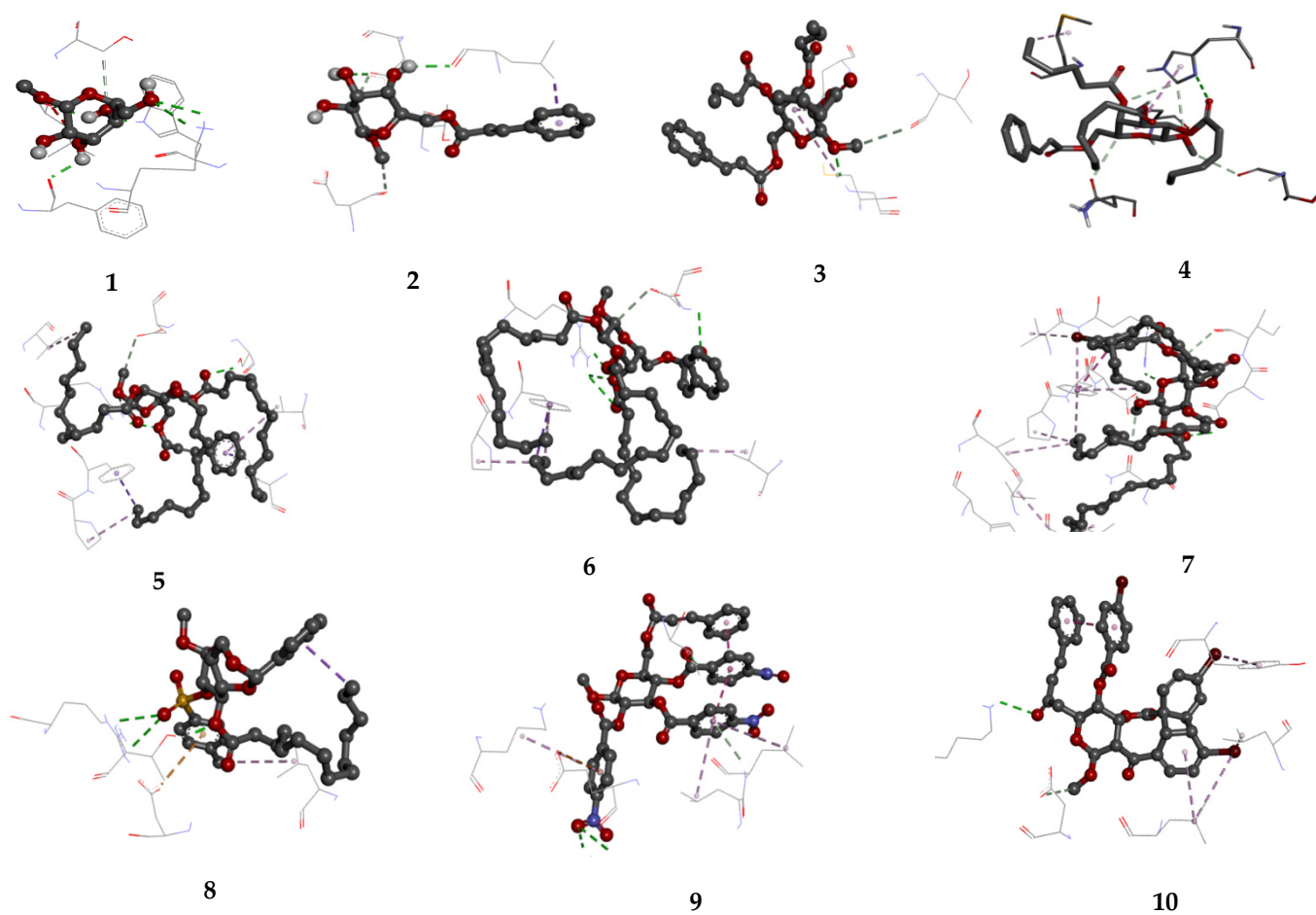
**Figure S8.** Protein-ligand interactions of all compounds.
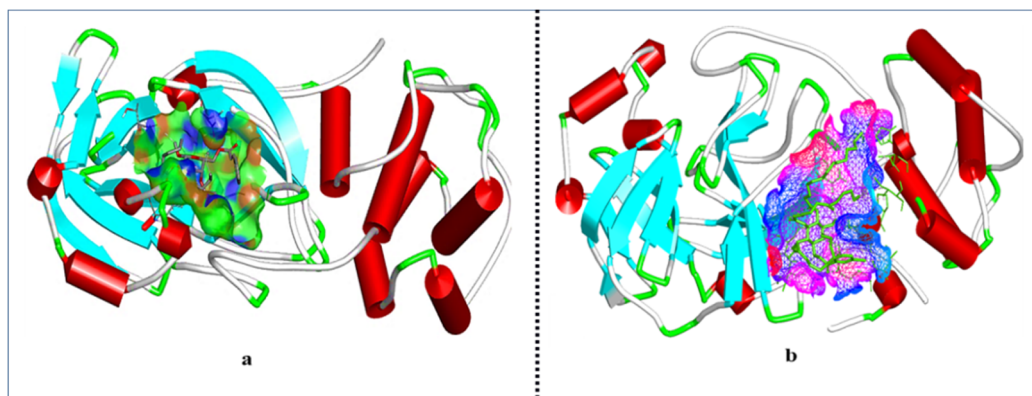
**Figure S9.** Hydrogen bond surface (**a**) and hydrophobic surface (**b**) of 6Y84 with analog (**7**).
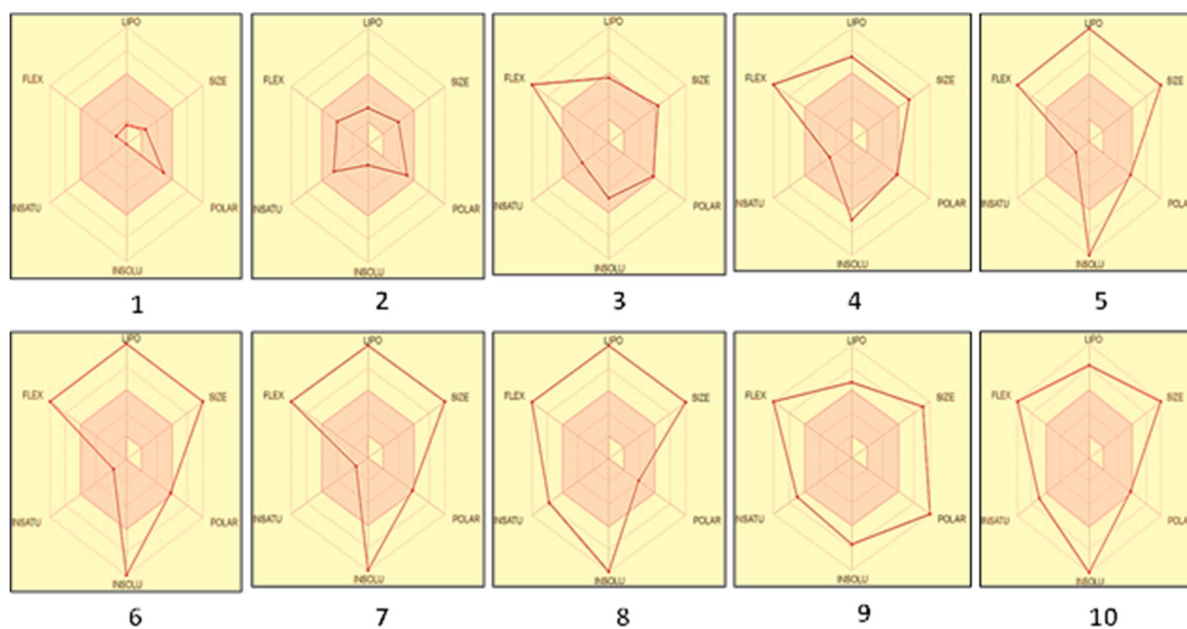
**Figure S10.** Bioactivity radar Charts of the MGP analogs where FLEX: Flexibility, LIPO: Lipophilicity, INSATU: Insaturation and INSOLU: Insolubility.
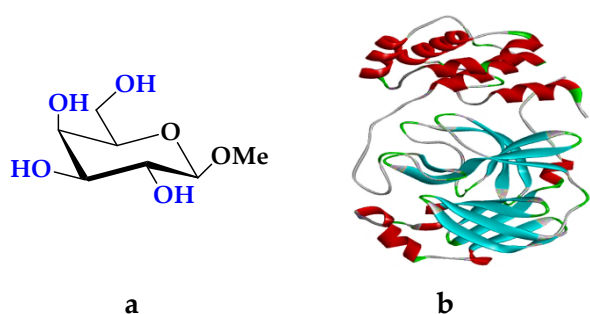
**Figure S11.** (**a**); 2D structure of MGP and (**b**); crystal structure of SARS-CoV-2 main protease (PDB: 6Y84).
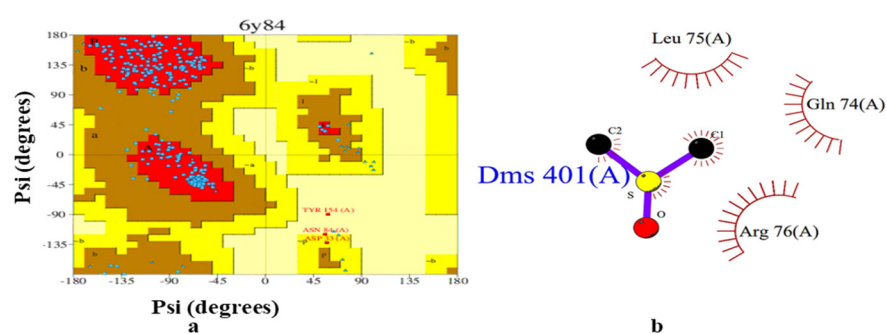


**Figure S12.** (**a**); Ramachandran plot for the SARS-CoV-2 main protease (PDB: 6Y84) (**b**); LigPlot image of the SARS-CoV-2 main protease (PDB: 6Y84) complex in 2D view predicted by PDBsum.

**Table S1:** Prediction of antimicrobial activity of the MGP analogs using PASS.

| Biological Activity | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Compound no. | Antibacterial | | Antifungal | | Antioxidant | | Anti-carcinogenic | |
| | Pa | Pi | Pa | Pi | Pa | Pi | Pa | Pi |
| 1 | 0.541 | 0.013 | 0.628 | 0.016 | 0.403 | 0.041 | 0.731 | 0.008 |
| 2 | 0.530 | 0.014 | 0.672 | 0.011 | 0.647 | 0.004 | 0.834 | 0.004 |
| 3 | 0.549 | 0.012 | 0.702 | 0.010 | 0.518 | 0.006 | 0.737 | 0.007 |
| 4 | 0.551 | 0.012 | 0.713 | 0.009 | 0.515 | 0.006 | 0.739 | 0.007 |
| 5 | 0.551 | 0.012 | 0.713 | 0.009 | 0.515 | 0.006 | 0.739 | 0.007 |
| 6 | 0.551 | 0.012 | 0.713 | 0.009 | 0.515 | 0.006 | 0.739 | 0.007 |
| 7 | 0.551 | 0.012 | 0.713 | 0.009 | 0.515 | 0.006 | 0.739 | 0.007 |
| 8 | 0.433 | 0.024 | 0.612 | 0.017 | 0.506 | 0.006 | 0.578 | 0.014 |
| 9 | 0.550 | 0.017 | 0.654 | 0.013 | 0.478 | 0.008 | 0.644 | 0.011 |
| 10 | 0.520 | 0.015 | 0.657 | 0.013 | 0.488 | 0.007 | 0.598 | 0.013 |

**Table S2.** Molecular formula, molecular weight, electronic energy (*E*), enthalpy (*H*), Gibb's free energy (*G*) in Hartree, and dipole moment (*μ*, Debye) of MGP analogs.

| Compound no. | MF | MW | E | H | G | μ |
|---|---|---|---|---|---|---|
| 1 | $C_7H_{14}O_6$ | 194.18 | –722.2093 | –722.2084 | –722.2608 | 4.7712 |
| 2 | $C_{16}H_{20}O_7$ | 324.33 | –1141.5888 | –1141.5878 | –1141.6641 | 4.2649 |
| 3 | $C_{28}H_{38}O_{10}$ | 534.60 | –1831.3718 | –1831.3709 | –1831.4881 | 5.9289 |
| 4 | $C_{34}H_{50}O_{10}$ | 618.75 | –2065.7868 | –2065.7859 | –2065.9235 | 5.7353 |
| 5 | $C_{52}H_{86}O_{10}$ | 874.25 | –2769.0296 | –2769.0286 | –2769.2223 | 4.8235 |
| 6 | $C_{58}H_{98}O_{10}$ | 955.39 | –3005.1369 | –3005.1358 | –3005.4269 | 3.1229 |
| 7 | $C_{64}H_{110}O_{10}$ | 1039.55 | –3418.2109 | –3418.2103 | –3418.8237 | 4.6329 |
| 8 | $C_{73}H_{62}O_7$ | 1051.29 | –3719.9182 | –3719.9172 | –3719.9961 | 5.2934 |
| 9 | $C_{37}H_{29}O_{16}N_3$ | 771.64 | –2778.8441 | –2778.8432 | –2778.9831 | 5.6946 |
| 10 | $C_{37}H_{29}O_{10}Br_3$ | 873.33 | –9702.7449 | –9702.7440 | –9702.8701 | 6.4697 |

**Table S3.** Energy (eV) of HOMO, LUMO, Gap (Δ), hardness ($\eta$), softness ($S$), and chemical potential ($\mu$) of MGP analogs.

| Compound no. | HOMO | LUMO | Gap ($\Delta\varepsilon$) | $\eta$ | $S$ | $\mu$ |
|---|---|---|---|---|---|---|
| 1 | −6.1918 | 1.3761 | 7.5679 | 3.7839 | 0.2643 | −2.4078 |
| 2 | −6.5306 | −1.8074 | 4.7232 | 2.3616 | 0.4234 | −4.1690 |
| 3 | −6.3169 | −1.6378 | 4.6791 | 2.3395 | 0.4274 | −3.9773 |
| 4 | −6.8035 | −2.1736 | 4.6299 | 2.3149 | 0.4319 | −4.4885 |
| 5 | −6.6112 | −1.9140 | 4.6972 | 2.3486 | 0.4257 | −4.2626 |
| 6 | −6.4647 | −1.7998 | 4.6649 | 2.3324 | 0.4287 | −4.1322 |
| 7 | −6.9234 | −1.4123 | 5.5111 | 2.7555 | 0.3629 | −4.1678 |
| 8 | −6.3212 | −1.8312 | 4.4900 | 2.2450 | 0.4454 | −4.0762 |
| 9 | −6.6925 | −3.5391 | 3.1534 | 1.5767 | 0.6342 | −5.1158 |
| 10 | −5.9226 | −2.2964 | 3.6262 | 1.8131 | 0.5515 | −4.1095 |

**Table S4.** Prediction of in silico of metabolism of MGP analogs.

| Compound no. | Cyp1A2 | Cyp2C19 | Cyp2D6 | Cyp3A4 |
|---|---|---|---|---|
| 1 | No | No | No | No |
| 2 | No | No | No | No |
| 3 | No | No | No | Yes |
| 4 | No | No | No | Yes |
| 5 | No | No | No | Yes |
| 6 | No | No | No | Yes |
| 7 | No | No | No | Yes |
| 8 | No | No | No | Yes |
| 9 | No | No | No | Yes |
| 10 | No | No | No | Yes |

**Table S5.** Prediction in silico of toxicity of MGP analogs.

| Compound no. | Ames toxicity | Herg1 inhibition | LD50 | Skin sensitization |
|---|---|---|---|---|
| 1 | No | No | 1.533 | No |
| 2 | yes | No | 2.471 | No |
| 3 | No | No | 2.564 | No |
| 4 | No | No | 2.337 | No |
| 5 | No | No | 2.410 | No |
| 6 | No | No | 2.452 | No |
| 7 | No | No | 2.472 | No |
| 8 | No | No | 2.482 | No |
| 9 | No | No | 2.485 | No |
| 10 | No | No | 2.657 | No |