# Supplementary Information

## MS analyses

**Table S1.** Mass spectrometric analysis of γ-oryzanol components.

| Compound | m/z (-) | Retention vol (mL) | Relative abundance (%) |
|---|---|---|---|
| CAF | 601.79 | 6.2 | 58 |
| 24MCAF | 615.80 | 6.95 | 58 |
| SF | 589.76 | 7.3 | 23 |
| CampF | 575.76 | 8.3 | 27 |

## Molecular docking

**Table S2**. Amino acids constituting the predicted binding interfaces to human HMGCR. Discriminating amino acids are coloured in red.

| Compound | Amino acids of the binding interface | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cycloartenyl ferulate | His488 | Ser520 | Leu521 | | | Ala525 | Gly566 | Arg627 | Ala654 | Met657 | Asn658 | Met659 | Gly806 | Gly807 | Asn810 |
| 24-methyleneCF | His488 | Ser520 | Leu521 | Met523 | | | Gly566 | Arg627 | Ala654 | Met657 | Asn658 | Met659 | Gly806 | Gly807 | Asn810 |
| β-sitosteryl ferulate | His488 | Ser520 | | Met523 | Gly524 | Ala525 | Gly566 | Arg627 | Ala654 | Met657 | Asn658 | Met659 | Gly806 | Gly807 | Asn810 |
| Campesteryl ferulate | His488 | Ser520 | | Met523 | Gly524 | Ala525 | Gly566 | Arg627 | Ala654 | Met657 | Asn658 | Met659 | Gly806 | Gly807 | Asn810 |

## Cell viability assessment

HepG2 cells were treated for 24 h with increasing concentrations of γ-oryzanol (ORY), CAF and 24MCAF and the MTT assay was performed to evaluate cell viability. No visible signs of toxicity were detected in HepG2 cells treated with even with the highest concentrations of γ-oryzanol used. Conversely, isolated CAF and 24MCAF displayed significant toxicity yet at 10 μg/mL.

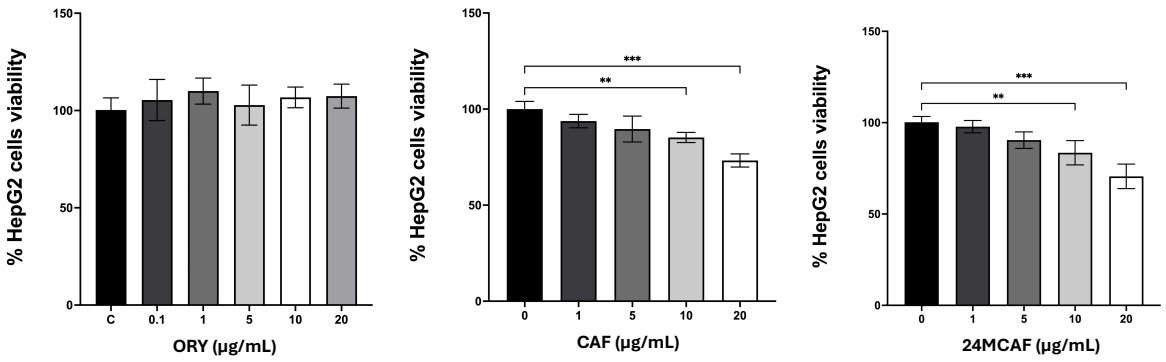



**Figure S1. HepG2 cells viability upon γ-oryzanol, CAF and 24MCAF treatment.** Cells were seeded on 96 well plates and treated as described in the Material and Methods section. The MTT assay was performed to check for cell viability. Asterisks indicate data points statistically significant with respect to the control (**p<0.01, ***p<0.001).

## Cholesterol quantification

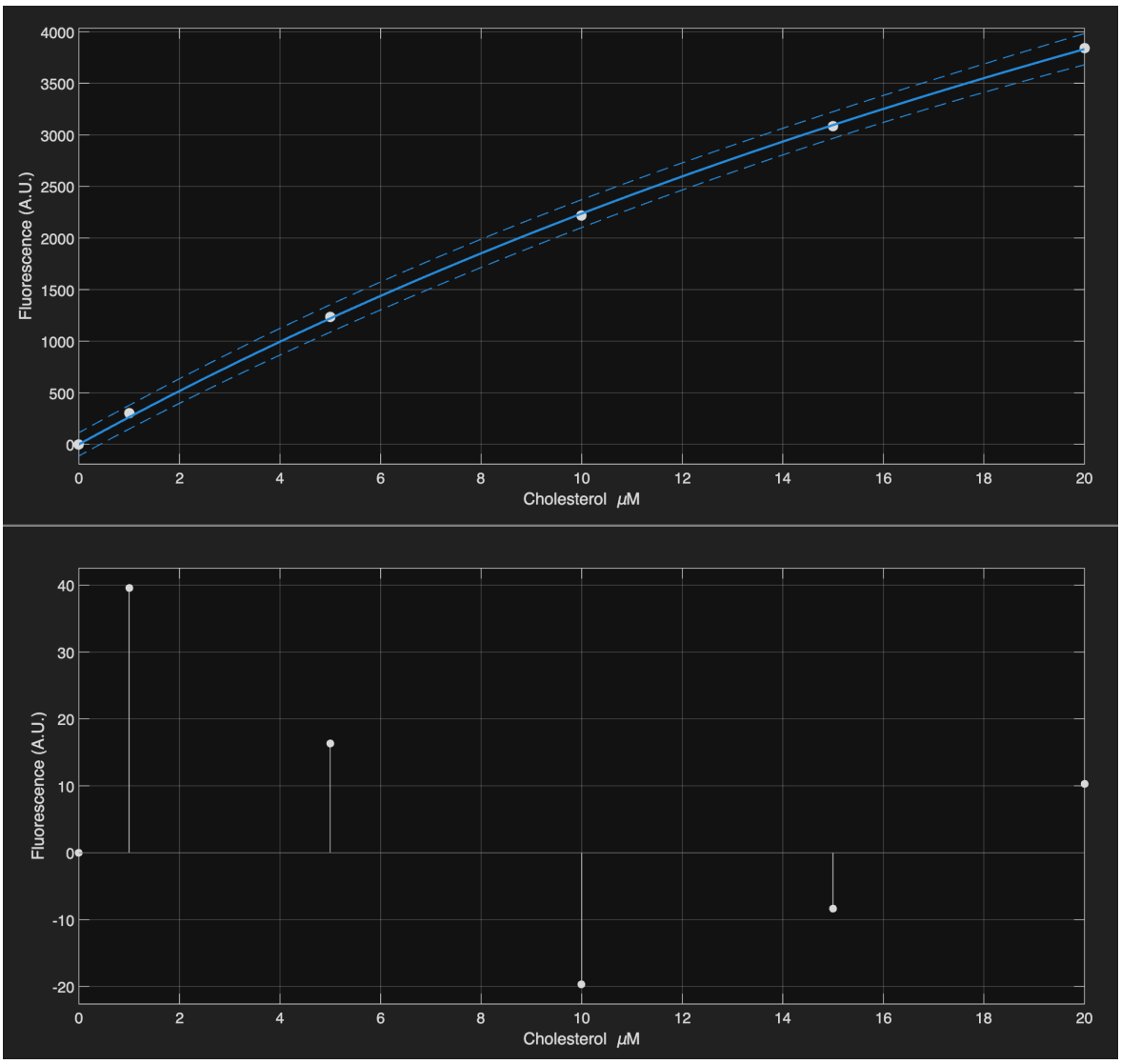
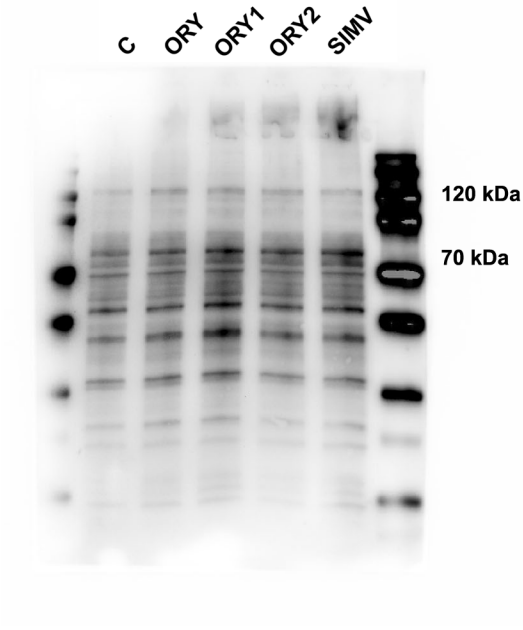



**Figure S2.** Cholesterol calibration curve (Upper panel) and residuals plot (Lower panel).

**Uncropped western blotting images**

**Figure 6 of the manuscript (part1)**

**SREBP2 mature (70 kDa) and precursor (120 kDa) forms.**




**LDLR**

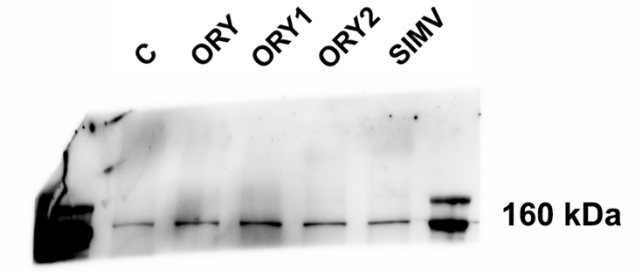
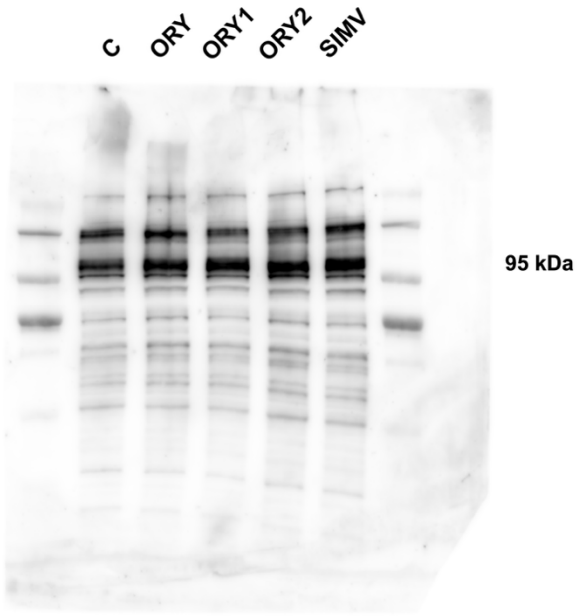


**Figure 6 of the manuscript (part2)**

**HMGCR**




**β-Actin**

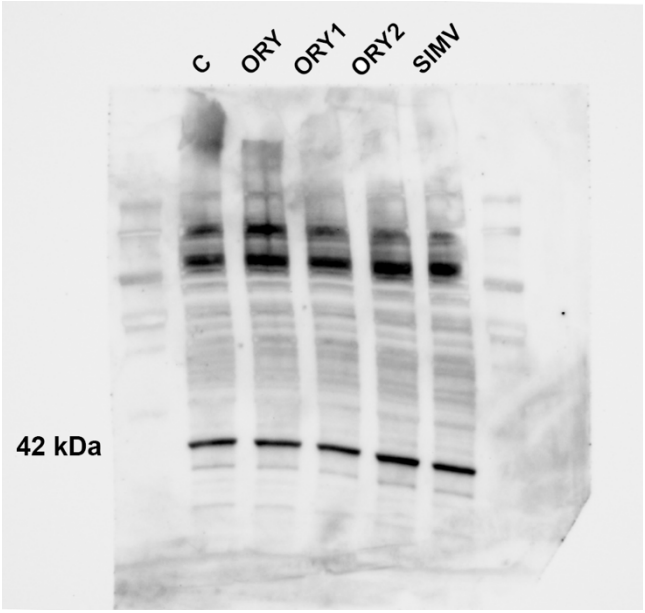
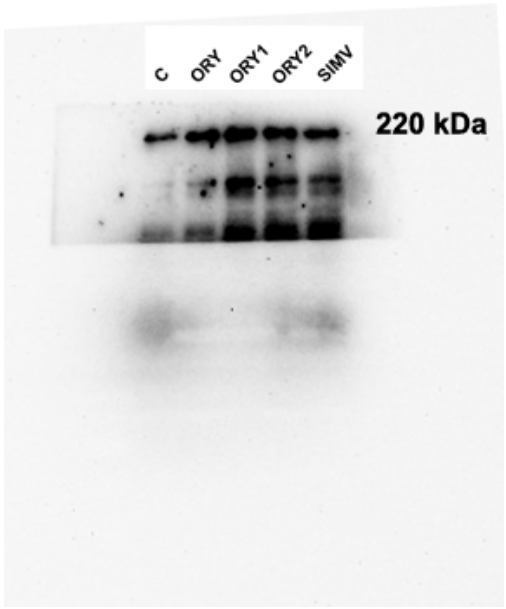


**Figure 7 of the manuscript (part1)**

**ABCA1**




**ABCG1**

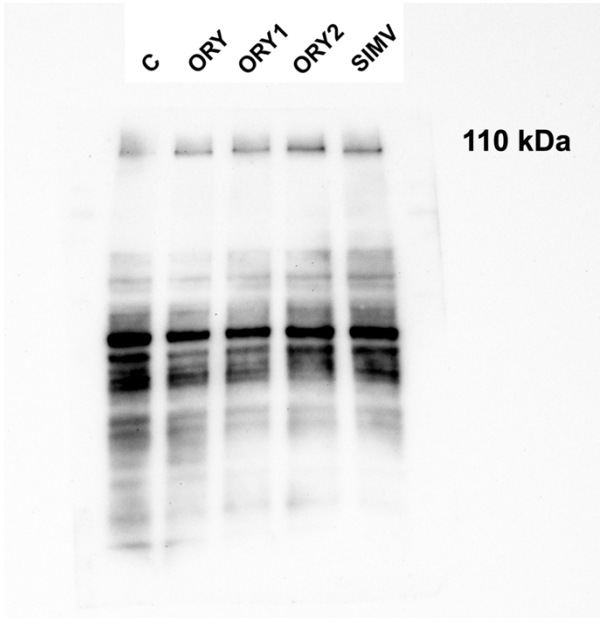
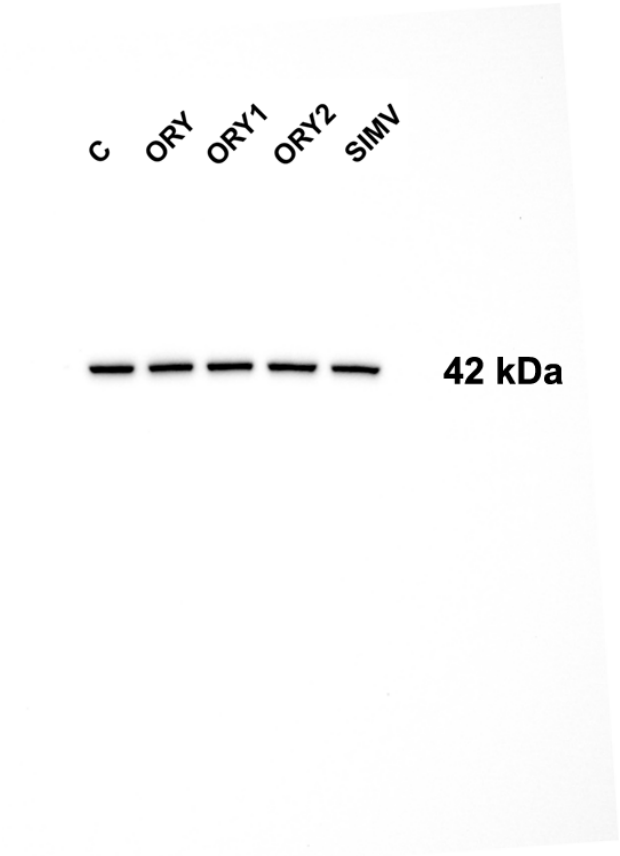


**Figure 7 of the manuscript (part2)**

**β-Actin**




**CYP7A1 (58 kDa) and β-Actin (42 kDa)**