Targeting MHC regulation using polycyclic polyprenylated acylphloroglucinols isolated from Garcinia *bancana*

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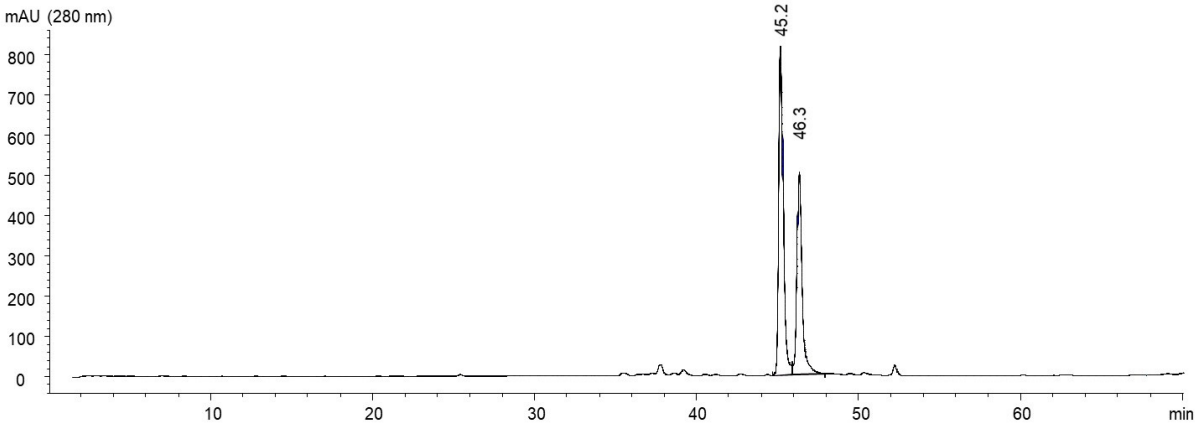

Figure S1. HPLC-UV (λ_{max} 280 nm) chromatogram of **GX** from *Garcina bancana* (bark) dichloromethanic extract (Batch KL4967). Guttiferone F (**3**, t_R = 45.2 min) represents 59.6% and xanthochymol (**2**, t_R = 46.3 min) 40.4% at 280 nm.

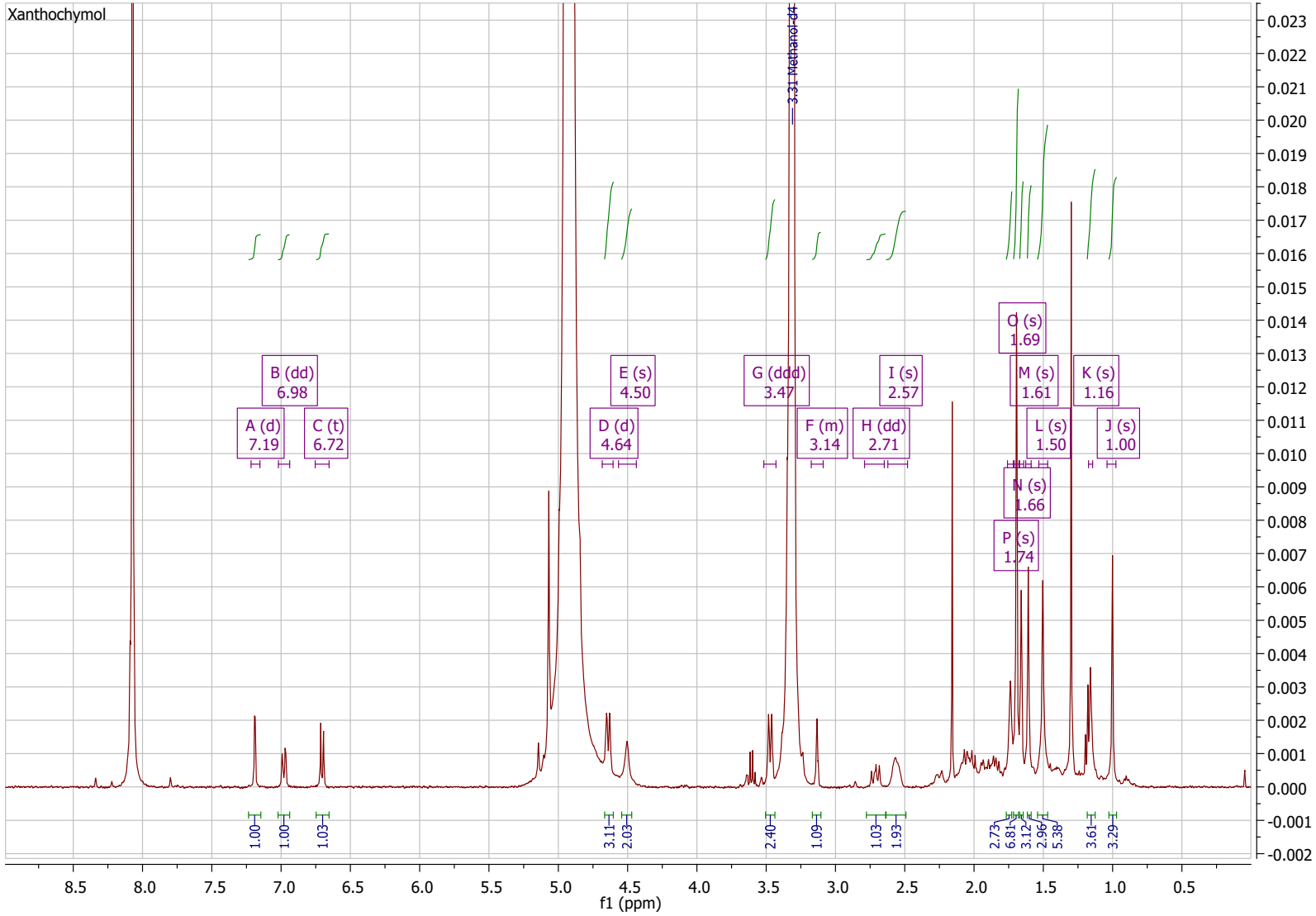

Figure S2. [1]H-NMR spectrum of xanthochymol **2** recorded in methanol-d4 +0.1% deuterated TFA at 400 MHz.

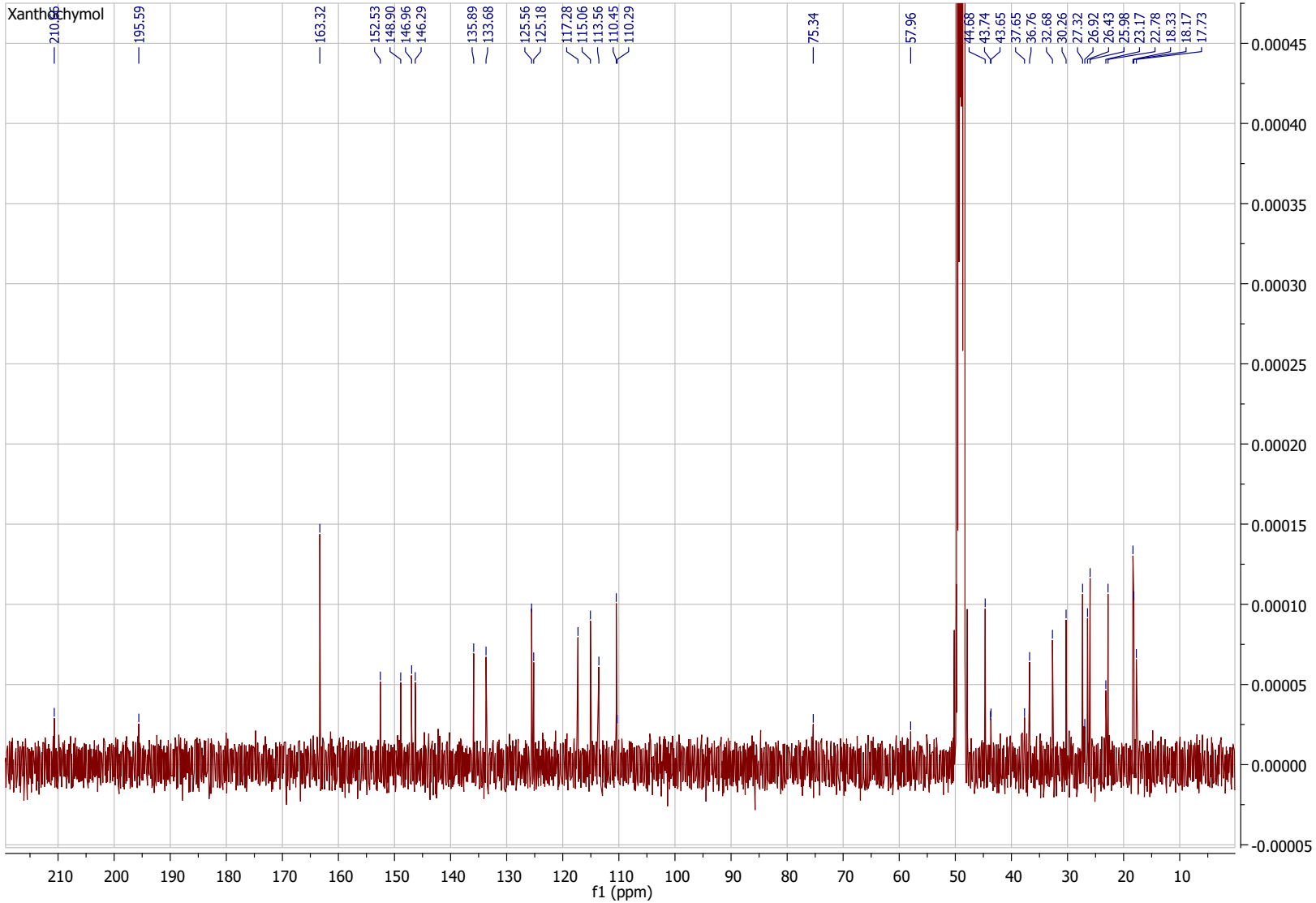

Figure S3. ^{13}C-NMR spectrum of xanthochymol **2** recorded in methanol-d4 +0.1% deuterated TFA at 100 MHz.

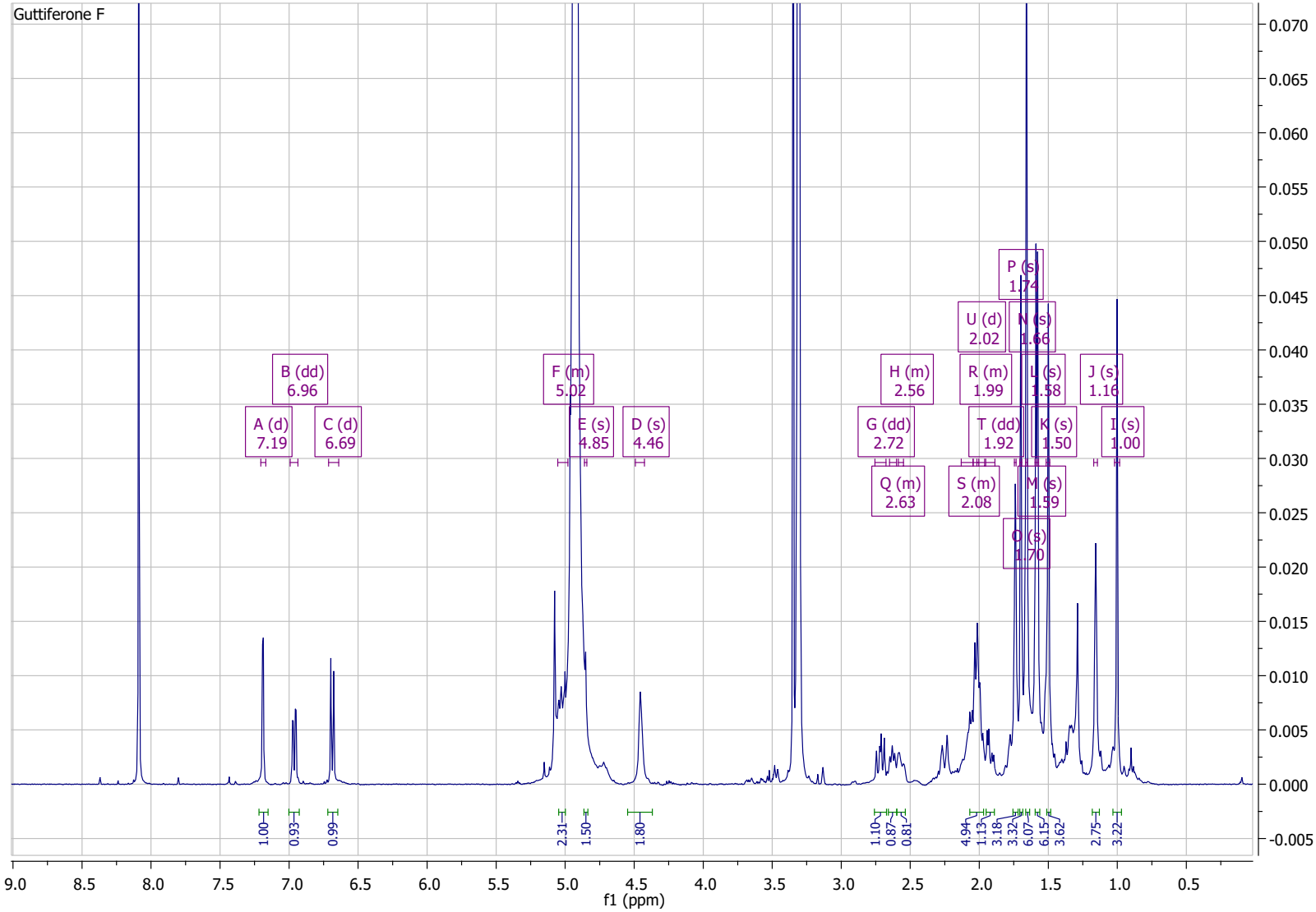

Figure S4. [1]H-NMR spectrum of guttiferone F **3** recorded in methanol-d4 +0.1% deuterated TFA at 400 MHz.

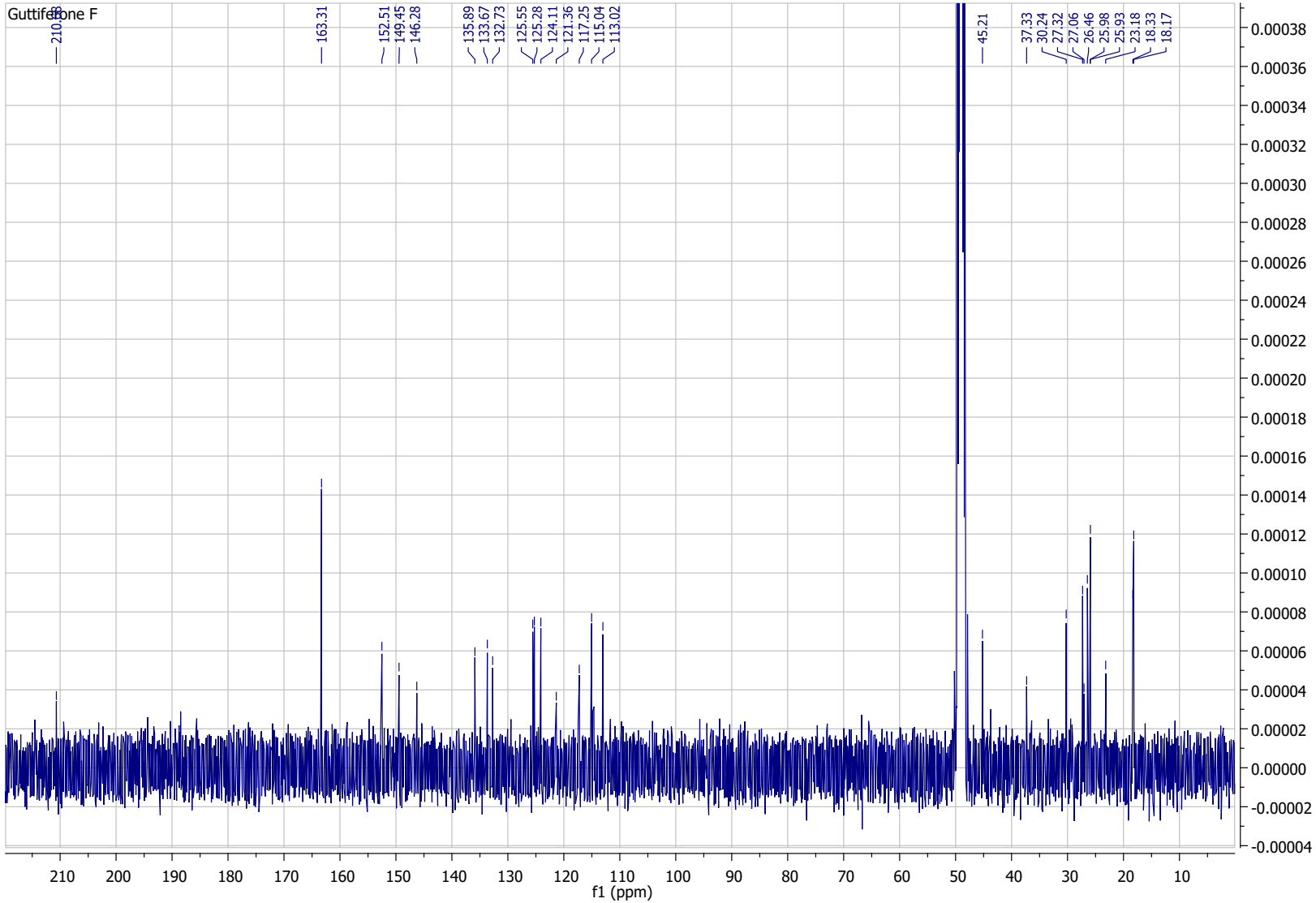

Figure S5. ^{13}C-NMR spectrum of guttiferone F **3** recorded in methanol-d4 +0.1% deuterated TFA at 100 MHz.

Confluent EC monolayers were incubated with diluent only as a negative control, simvastatine or zoledronic acid (ZA) at 10 μM in the absence (unstimulated endothelial cells) or in the presence (+ IFNγ) of IFNγ (100 U/mL) for 48 h. Cells were harvested, subjected to immunolabeling with specific antibodies against HLA class I, HLA class II, HLA-E and MICA and analyzed by flow cytometry. Data are depicted as histograms of fluorescence intensity (x-axis) versus cell number (y-axis) for MHC molecules (red) and for controls (irrelevant isotype control antibodies, grey). Geometric means of fluorescence are indicated in red.

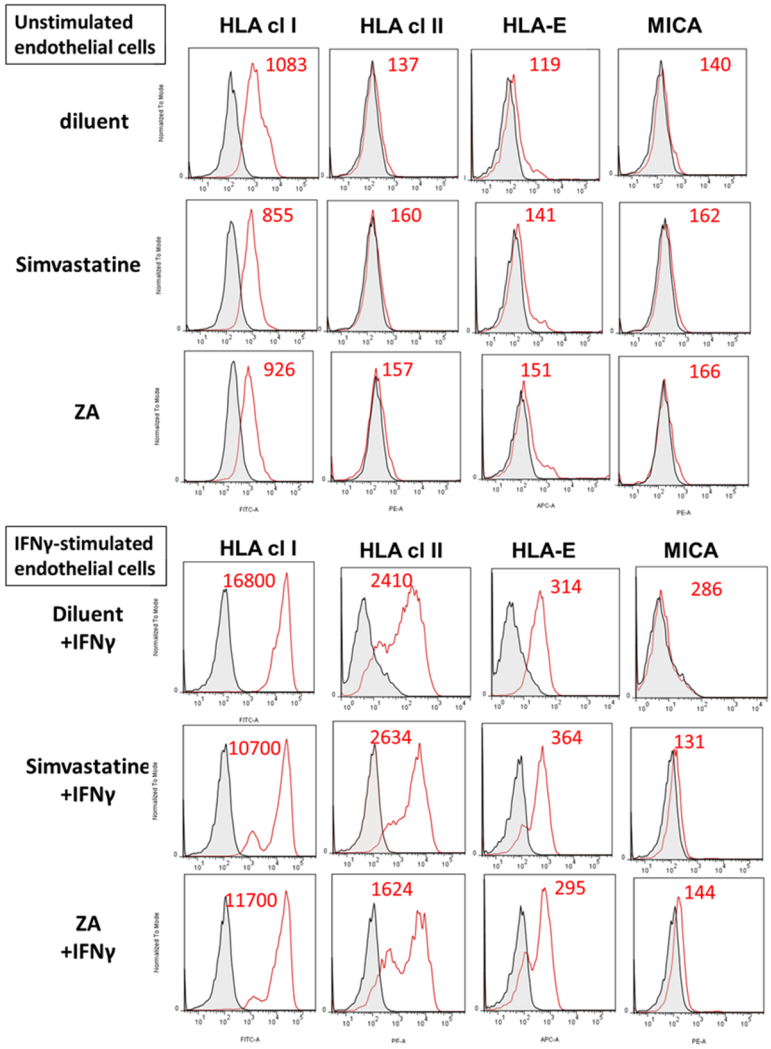

Figure S6. Effect of Simvastatine and Zoledronic acid (ZA) on the expression of MHC molecules.

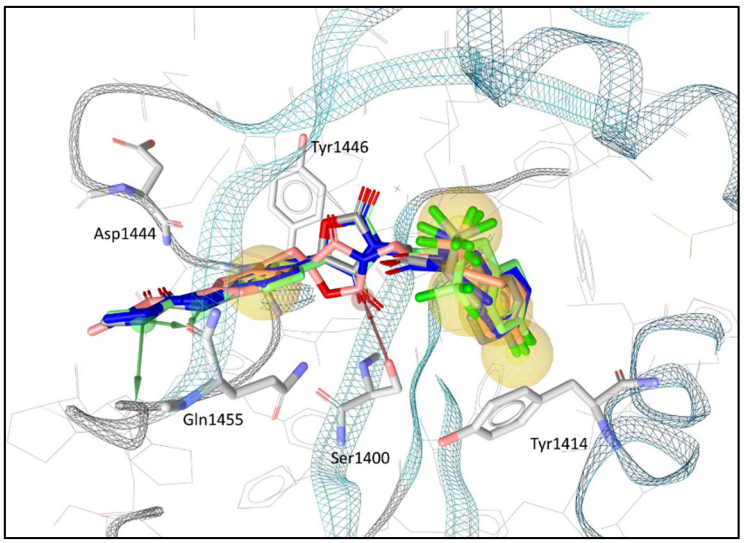

Figure S7. Superimposes of the original structure A-485 and its energy-minimized conformation as well as the rebuilt structure in the binding site of histone acetyltransferase p300. Red and green arrows represent hydrogen bond acceptors and donors, respectively; and yellow spheres show the hydrophobic contacts between the ligands and the protein.

Table S1. *Garcinia* species from Malaysia (name, voucher number and available organs) and data on their phytochemistry.

***Garcinia* species**	**Voucher number** (KL, Kuala Lumpur) and **organs** (**B** = bark, **L** = leaf, **Fr** = fruit)	**Data on phytochemistry**	
		Secondary metabolites previously described	Presence of PPAPs as major products in DCM extracts according to LC-UV-MS²*
G. bancana Miq.	**4967** (B, L, Fr), **5033** (B, L)	Biphenyls, PPAPs, flavonoids, triterpènes [1]	B and L: Yes
G. cowa Roxb.	**4587**, **5526** (B, L)	Biphenyls, xanthones, flavonoids, terpenes [2]	NA
G. diversifolia King	**5712** (B, L)	Triterpenes [3]	NA
G. dumosa King	**5516** (B, L)	-	No (undetermined)
G. brevirostris Scheff. (= *G. eugeniaefolia* Wall.)	**4611**, **5074**, **5273**, **5456** (B, L), **5251** (B)	Benzophenones [4]	No (Tocotrienols)
G. forbesii King	**5146**, **5518** (B, L)	Xanthones [5]	NA
G. gaudichaudii Planch. & Triana	**5483** (B, L, Fr)	Xanthones [6]	NA
G. griffithii T. Anderson	**5303** (B, L)	Xanthones, PPAPs [7]	B: No (Xanthones) L: Yes
G. celebica L. (= *G. hombroniana* Pierre)	**4800** (B, L)	Triterpenes, xanthones, benzophenones, flavonoids [8]	No (Triterpenes)
G. nervosa Miq.	**5702** (B, L)	Flavonoids [9]	NA
G. nigrolineata Planch.	**5555** (B, L)	Biphenyls, xanthones [10]	NA
G. opaca King	**4532** (B, L, Fr), **4560** (B, L)	Xanthones [11], terpenes [12]	NA
G. opaca King **var. dumosa** Whitmore[a]	**5589** (B, L)		NA
G. parvifolia (Miq.) Miq.	**5073**, **5259** (B, L), **5248** (B), **5670** (B, L, Fr)	Flavonoids [13], phloroglucinols, depsidones, xanthones [14]	No (Xanthones)
G. prainiana King	**5661** (B, L)	Triterpenes, flavonoids [15]	NA
G. pyrifera Ridl.	**4523**, **4954**, **5443** (B, L)	PPAPs (fruits), xanthones (bark) [16]	NA
G. rostrata (Hassk.) Miq.	**5175** (B, L)	Xanthones [17]	NA

* Several products with λ_{max} around 230-235, 275-280 and 320 nm and a molecular weight between 560 and 618 Da [18]. NA : Not analyzed.

Table S2. ChemPLP scores for the top 10 poses in docking experiments.

Native ligand A-485	**Guttiferone J (1)**	**Xanthochymol (2)**	**Guttiferone F (3)**	**Garcinol (4)**
114.36	96.35	82.46	90.77	88.04
109.57	86.53	79.35	89.83	87.19
107.02	71.77	78.44	86.36	86.52
84.45	70.04	69.06	85.77	86.01
	69.41		83.31	84.63
	69.17		76.01	84.25
	68.04		74.99	83.87
	64.25		72.63	82.75
	64.21		71.99	81.23
	62.14		71.76	80.19

The cut-off cluster of docking poses was defined at 0.5 Å. For the energy-minimized reconstructed ligand (A-485) and xanthochymol, only four docked poses were obtained for each compound. This means other conformations were clustered in these best-docked poses.

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Abbreviations:

CIITA pIV: class II transactivator promotor IV
CBP: CREB binding protein
CREB: cAMP-responsive element binding protein
CsA: Cyclosporine A
DCM: dichloromethane
EC: endothelial cell
HAT: histone acetyltransferase
HDAC: histone deacetylase
HLA: human leukocyte antigen
IFNγ: interferon γ
IFNGR: IFNγ receptor
IRF9: IFN regulatory factor 9
JAK: Janus kinase
K: lysine
MHC: major histocompatibility complex
MICA: MHC class I-related chain A
NPs: natural products
PPAPs: polycyclic polyprenylated acylphloroglucinols
SAHA: suberoylanilide hydroxamic acid
Sim: simvastatin
SOCS: suppressor of cytokine signaling
STAT : signal transducer and activator of transcription
TNF: tumor necrosis factor
TSA: trichostatin A
Y: tyrosine
ZA: zoledronic acid