Supplementary data

1. Product Analysis

1.1. Thin layer Chromatography (TLC)

Analytical thin layer chromatography (TLC) was performed using Merck silica gel $60F_{254}$ plates and using diffrent optimized mobile phases. Chromatograms were observed under UV light, iodine, visualized by heating plates that were dipped in potassium permanganate ($KMnO_4$) reagent (3.0 g potassium permanganate, 20.0 g potassium carbonate, 5 mL NaOH (5%) and 300 mL distilled water).

1.2. Nuclear Magnetic Resonance Spectroscopy (NMR)

^{1}HNMR spectra were recorded at room temperature on the JOEL ECA, Japan 500 MHz at UPM. The ^{13}C NMR spectra were recorded on NMR (JOEL ECA, Japan) 125.7 MHz. Deuterated solvents (chloroform-D, methanol-D and DMSO) were obtained from Sigma-Alrich. Chemical shifts are reported in parts per million (ppm, δ) relative to internal tetramethylesilane (TMS, δ 0.0 ppm). The coupling constants (*J*) are expressed in Hz. The multiplicities of the signals are abbreviated as follows: s (singlet), d (doublet), t (triplet), dd (doublet of doublet), m (multiplet), etc.

1.3. Fourier-Transform Infrared Spectroscopy (FT-IR)

Fourier Transforms infrared spectroscopy (FTIR); Perkin Elmer Spectrum 100 was used for identification of functional groups. The IR spectrum was scanned in the wavelengthnumber range from 4000 cm^{-1} to 280 cm^{-1}.

1.4. Mass Spectrometry (MS)

Mass of compound *N*-acetyle-5-aminocalcylate has been recorded by GCMS QP2010 Plus SHIMADZU in UPM, and high resolution mass spectra (HRMS) acquired in the mass spectroscopy facilities at Malaysian genom institute through direct infuse mass spectrometry (DIMS). The sample was directly injected through a syringe pump (Havard apparatus, 11 plus, USA) into the electrospray ionization source (ESI). The mass spectrometry detection was performed using a ACQUITY® SQD with Single Quadrupole Detector (Waters Corporation, Milford, MA USA) operated in positive and negative ion electrospray modes. Nitrogen was used as desolvation gas. A centroid data collection mode was used in this analysis and the mass spectrometry system were controlled by MassLynx 4.1 software (Water).

Mass Spectrometry Parameters for DIMS		
Model/Brand	Waters Single Quadrupole Detector (SQD)	
Ion electrospray mode	**Positive**	**Negative**
Capillary voltage (kV)	3.2	2.8
Source temperature (◦C)	120	120
Extractor (V)	3.0	3.0
Cone gas flow (L/Hr)	50	50
Desolvation temperature (◦C)	250	250
Desolvation gas flow (L/Hr)	600	500

It should be noted that that the exact mass of compounds were calculated by BioChemDraw Ultra.

1.5. Melting point

Melting points were measured by Barnstead Electrothermal instrument

1.6. Yiled

The yield of products has been reported after isolating through column chromatograghy.

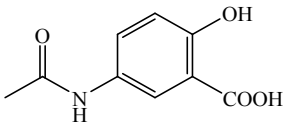
2. Characterization

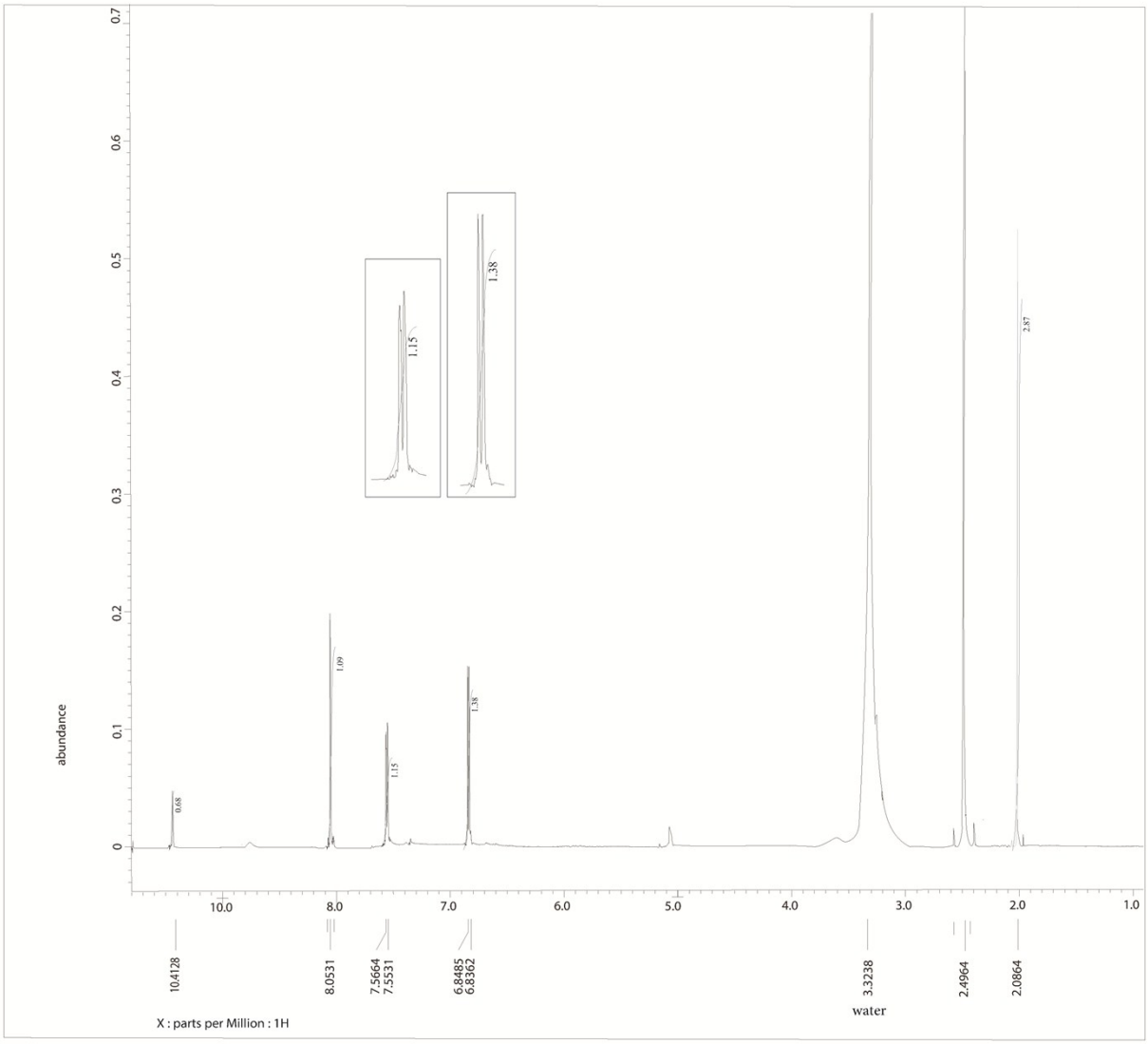
All NMR, FT-IR and Mass, yield and appearance data for each product are listed below.

2.1. 5-acetamido-2-hydroxy benzoic acid or *N*-acetyl-5-aminosalicylate (a)

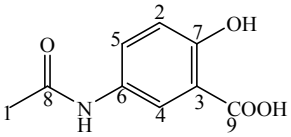
Yield: 67.5%. M.p: 195˚C. White, needle-shape crystals.

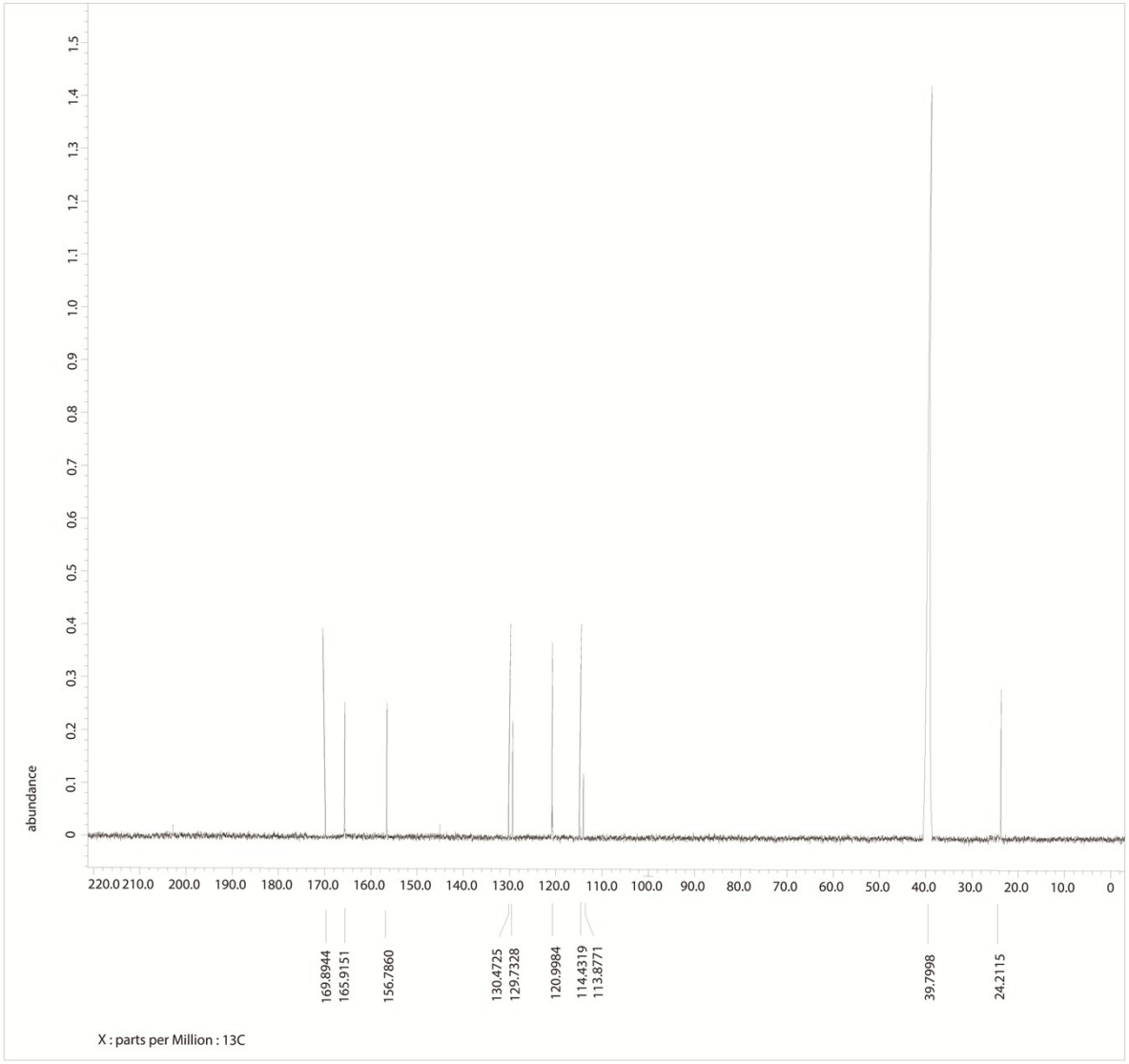
^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) = 2.08 (3H, CH_3), 6.83 (1H, d, *J*= 7.7 Hz, Ar-CH), 7.55 (1H, d, *J*= 7.9 Hz, Ar-CH), 8.05 (1H, s, Ar-CH), 10.41 (1H, s, COOH).





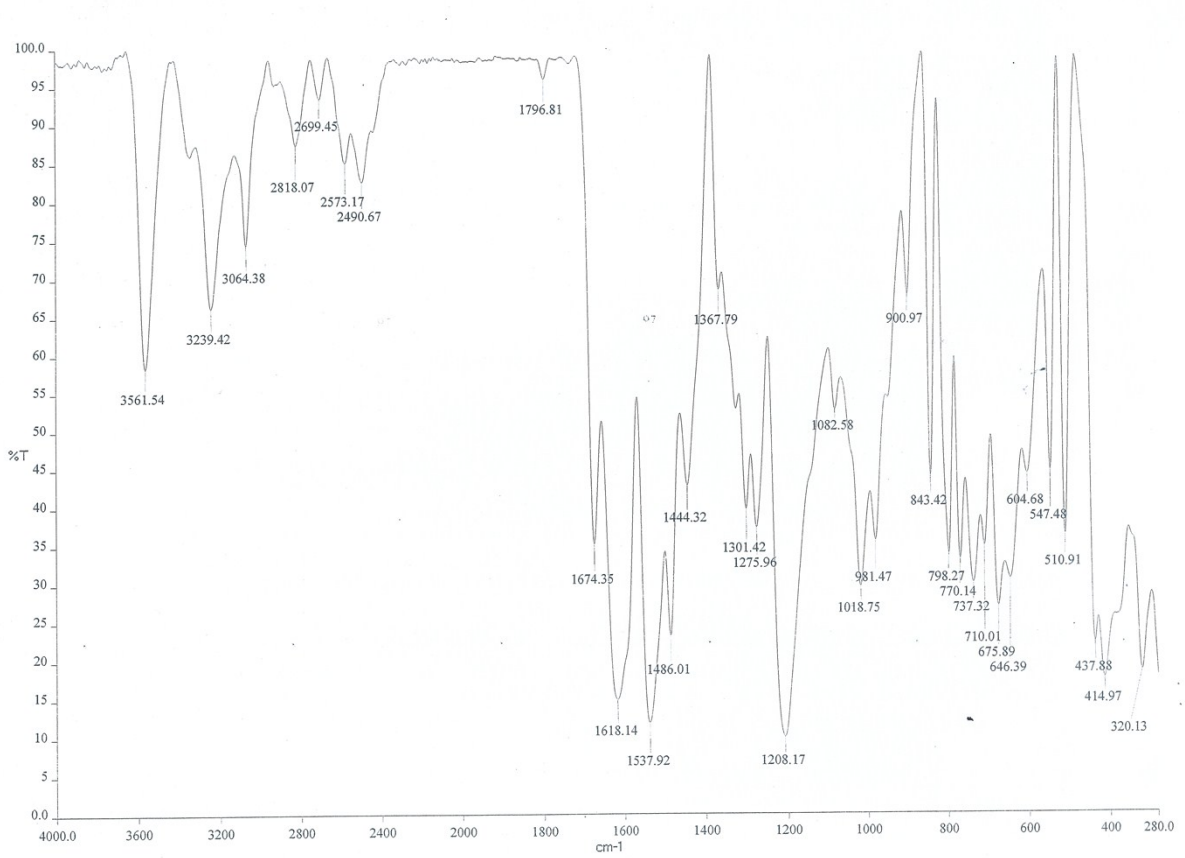
^{13}C NMR (125.8 MHz, DMSO-d_6) δ = 24.2 (C-1), 113.8, 114.4, 120.9, 129.7; (C-2, C-3, C-4, C-5), 130.4 (C-6), 156.7 (C-7), 165.9 (C-8), 169.8 (C-9).



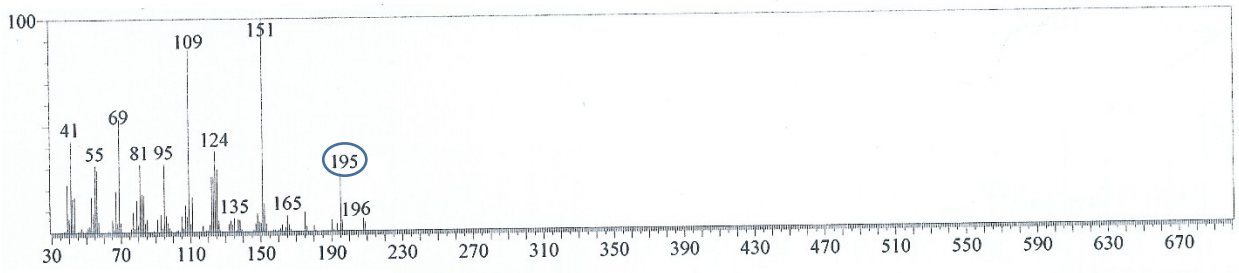


- As a reference for comparing characterization data of *N*-acetyl-5-aminosalicylate can be referred to reference **[56].** M. Nobilis, Z. Vybiralova, K. Sladkova, M. Lisa, M. Holčapek, J. Květina, *Journal of chromatography A*, **2006**, *1119*, 299-308.

FT-IR (ν): 3561, 3239, 3064, 2818, 2699, 2573, 2490, 1796, 1674, 1618, 1537, 1486, 1208, 1018.



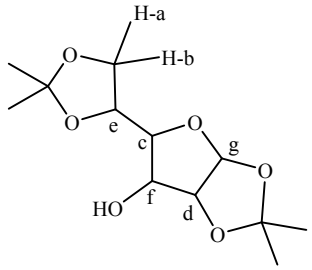
MS**:** GC- mass, $(M)^+$ m/z 195.0, [calcd; 195.053, formula ($C_9H_9NO_4$)].

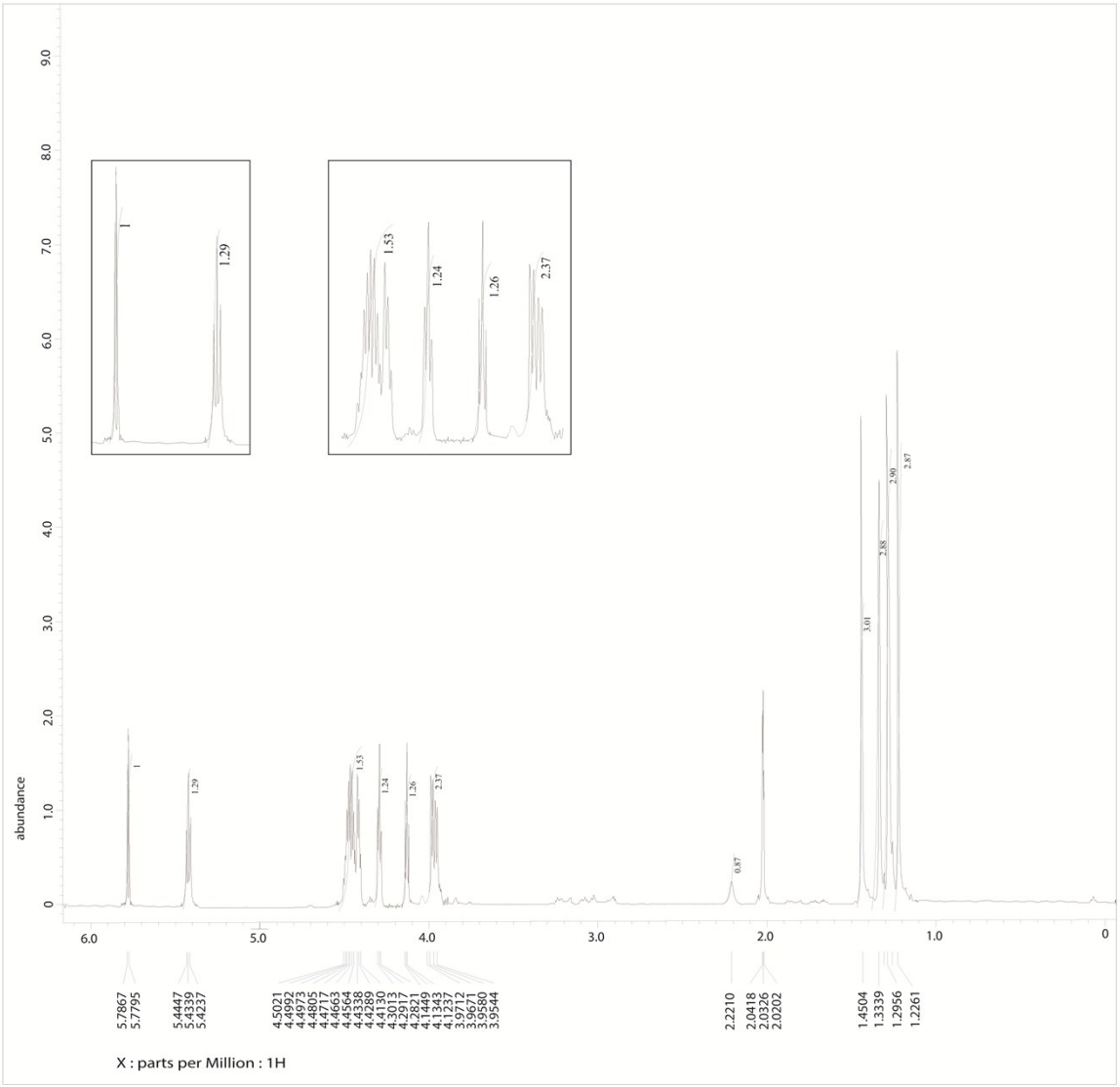


2.2. 1,2:5,6-Di-*O*-isopropylidene-D-glucfuranose or diacetone-glucose (b)

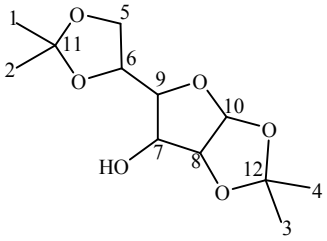
Yield: 61%. M.p: 109-110°C. White crystals. [α] 24/D -0.12, (c= 0.4 in acetone).

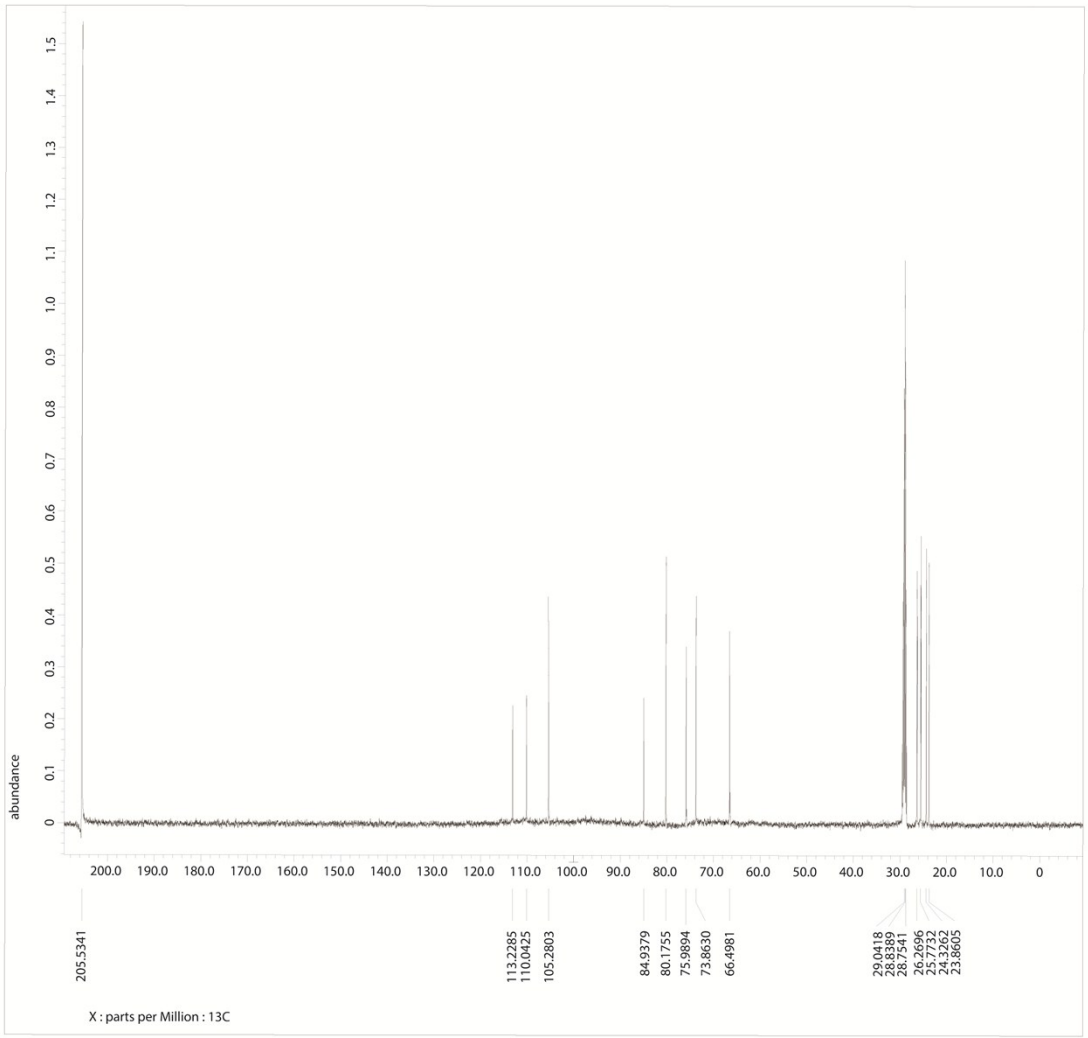
^{1}H NMR (500 MHz, acetone-d6): δ (ppm) = 1.22 (3H, s, CH3), 1.29 (3H, s, CH3), 1.33 (3H, s, CH3), 1.45 (3H, s, CH3), 2.22 (1H, s, OH), 3.95 (2H, dd, *J*= 6.3 Hz, *J*= 1.8 Hz, H-a, H-b), 4.12 (1H, t, *J*= 5.3 Hz, H-c), 4.28 (1H, t, *J*= 4.8 Hz, H-d), 4.41-4.50 (1H, m, H-e), 5.42 (1H, t, *J*= 5.1 Hz, H-f), 5.78 (1H, d, *J*= 3.6 Hz, H-g).





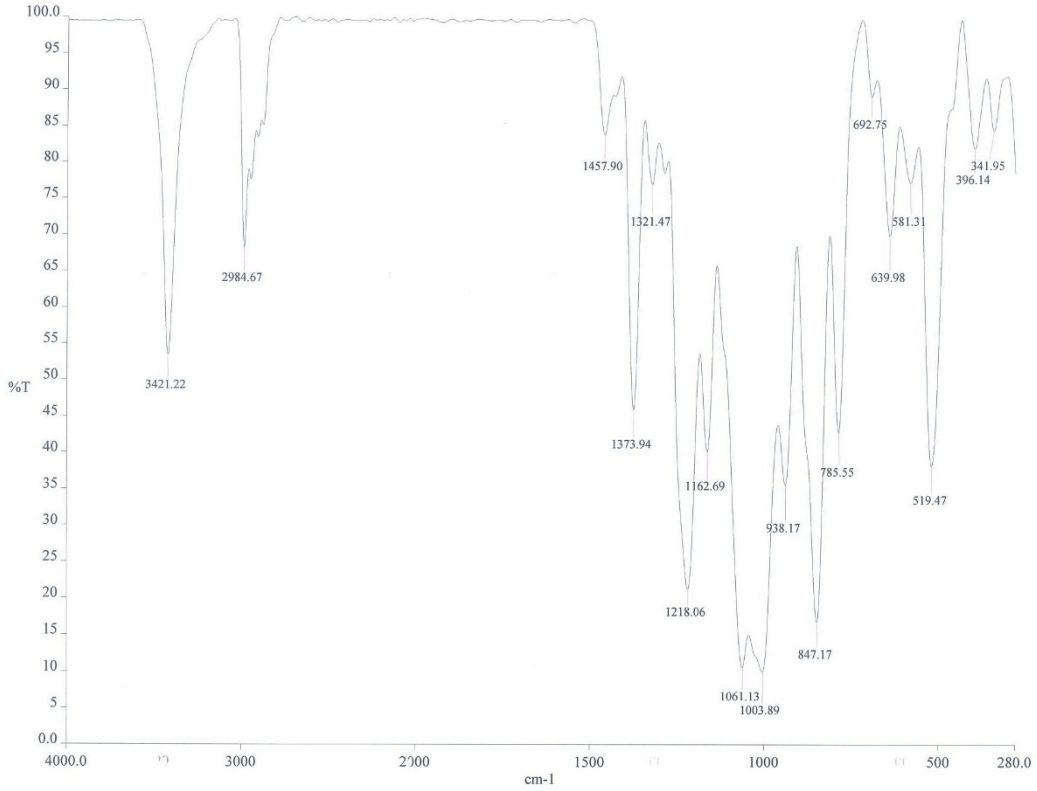
^{13}C NMR (125.8 MHz, acetone-d_6) δ = 23.8, 24.3, 25.7, 26.2; (C-1, C-2, C-3, C-4), 66.4 (C-5), 73.8 (C-6), 75.9 (C-7), 80.1 (C-8), 84.9 (C-9), 105.2 (C-10), 110.0 (C-11), 113.2 (C-12).



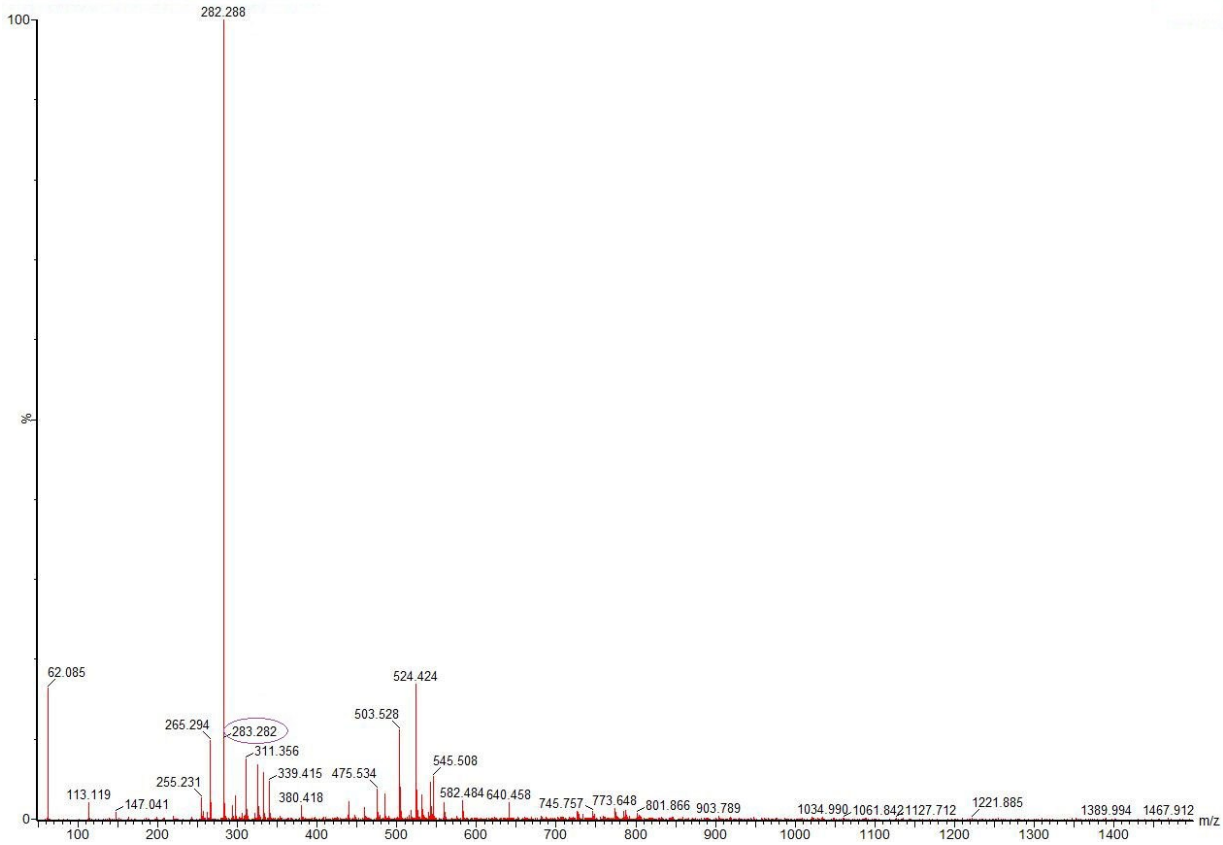


- As a reference for comparing characterization data of 1,2:5,6-di-Oisopropylidene-α-D-glucofuranose can be referred to reference **[39].** Y.W. Rong, Q.H. Zhang, W. Wang, B.L. Li, *Notes*, **2014**, *35*, 2165, and [40]. A.T. Khan,M. Musawwer Khan, *Carbohydrate Research*, **2010**, *345*, 154-159.

FT-IR (ν): 3421, 2984, 1457, 1373, 1321, 1218, 1162, 1061, 1003.



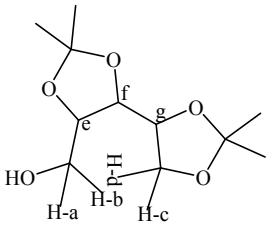
MS: HRMS $(M+Na)^+$, m/z 283.282, [calcd; 260.126, formula ($C_{12}H_{20}O_6$)].

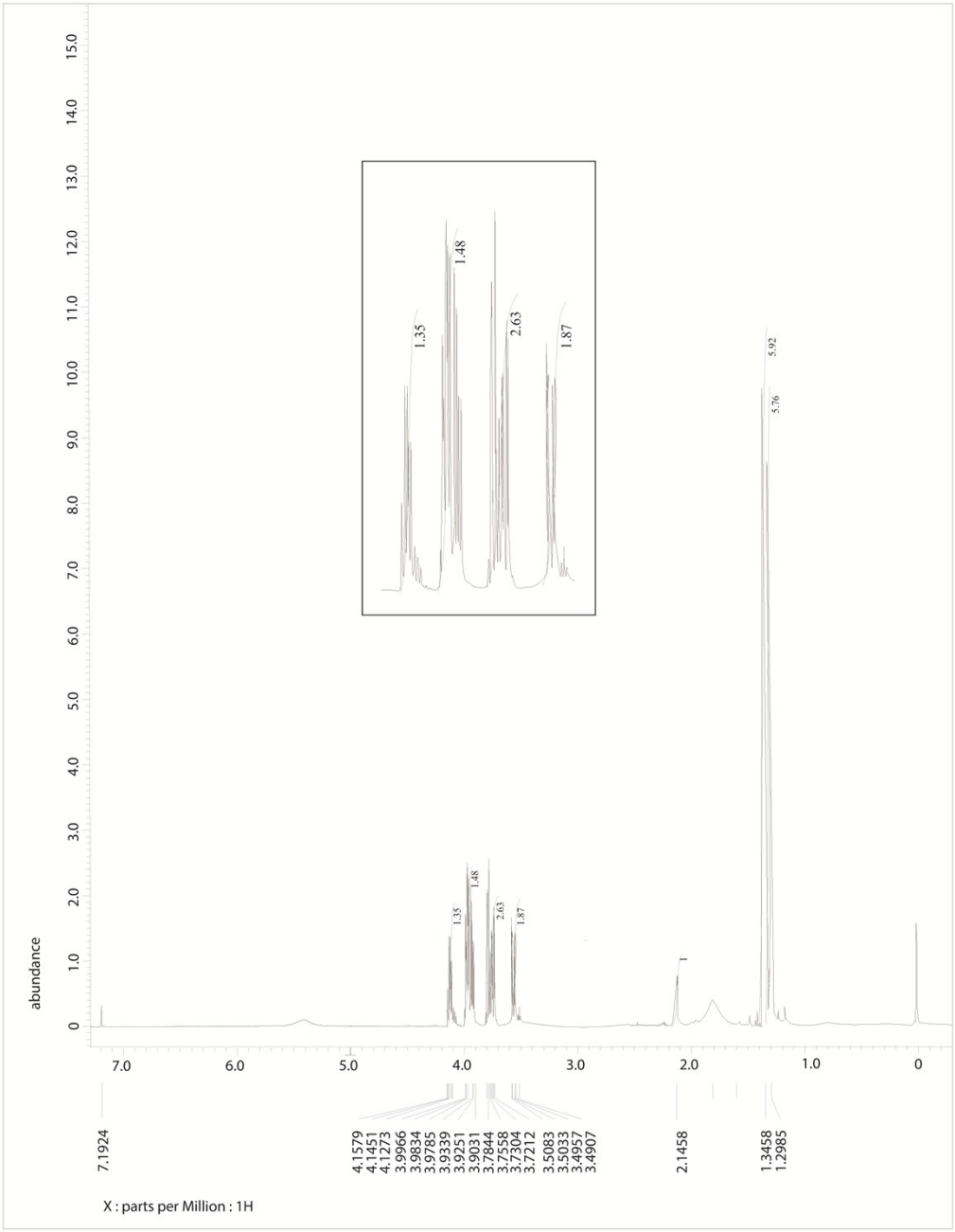


2.3. 2,3,4,5-Di-isopropylidene-D-xylitol or diacetone-xylitol (c)

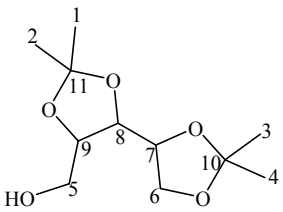
Yield: 57%. M.p: 30-33°C. White crystals. [α] 24/D -0.02, (c= 0.4 in acetone).

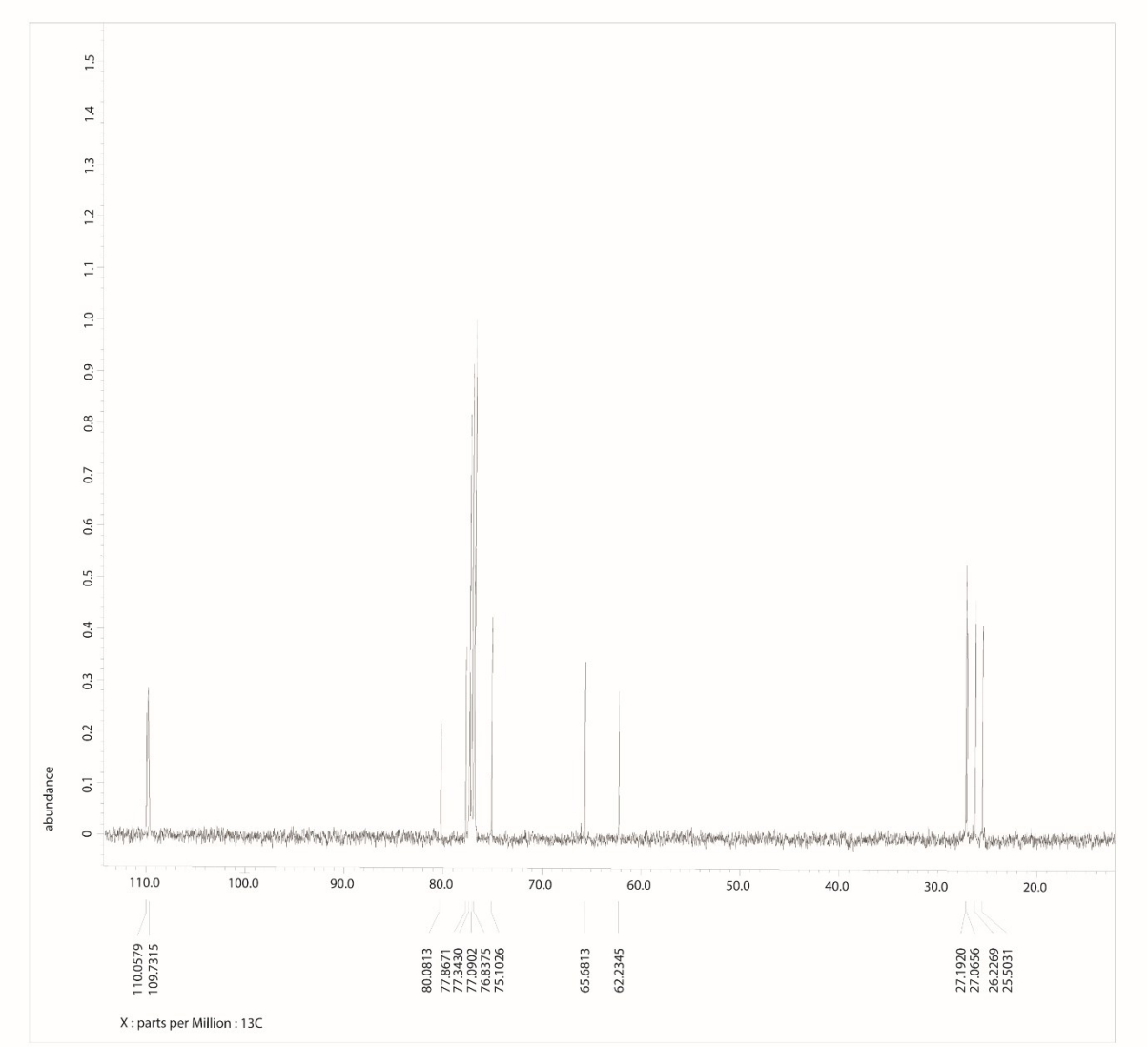
^{1}H NMR (500 MHz, chloroform-d_1): δ (ppm) = 1.29 (6H, s, 3 each, 2 × CH_3), 1.34 (6H, s, 3 each, 2 × CH_3), 2.14 (1H, s, OH), 3.49 (2H, dd, *J*= 6.3 Hz, *J*= 2.5 Hz, H-a, H-b), 3.72-3.78 (3H, m, H-c, H-d, H-e), 3.90-3.99 (1H, m, H-f), 4.12-4.15 (1H, m, H-g).





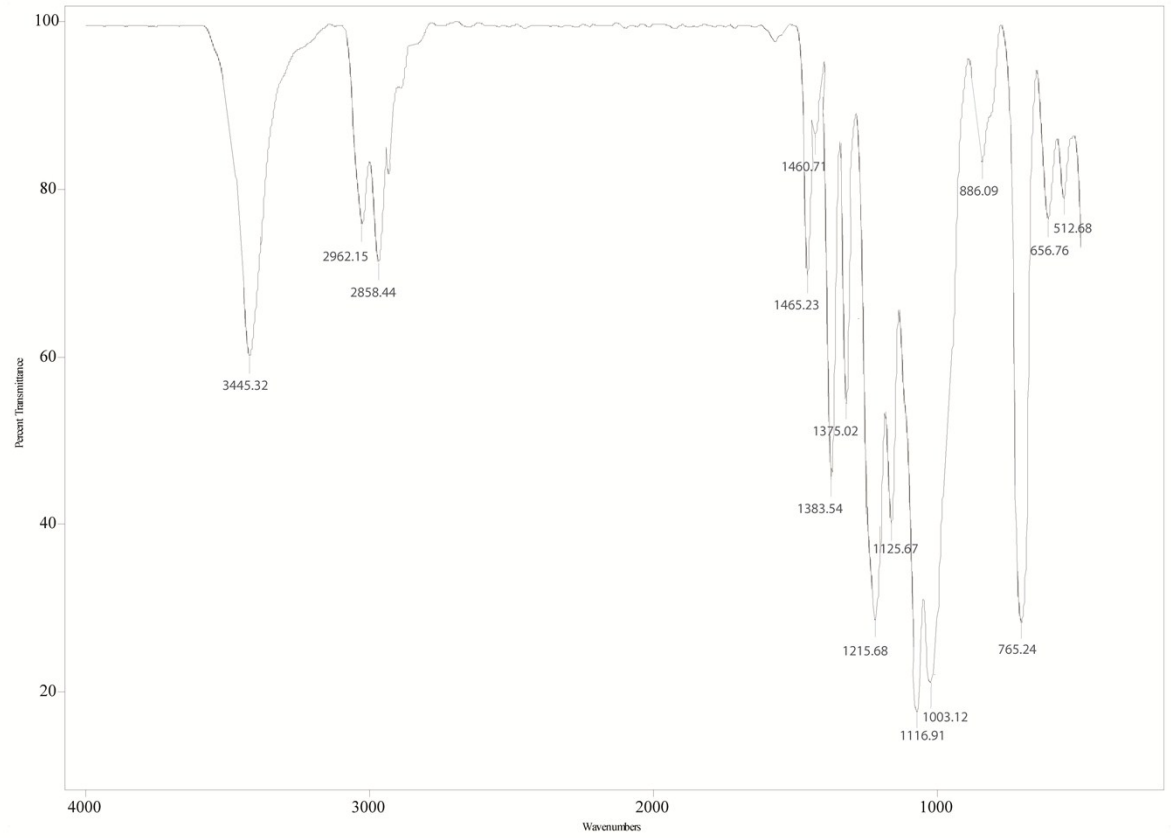
^{13}C NMR (125.8 MHz, chloroform-d_1) δ = 25.5, 26.2, 27.0, 27.1; (C-1, C-2, C-3, C-4), 62.2 (C-5), 65.6 (C-6), 75.1 (C-7, C-8), 77.8 (C-9), 109.7 (C-10), 110.05 (C-11).



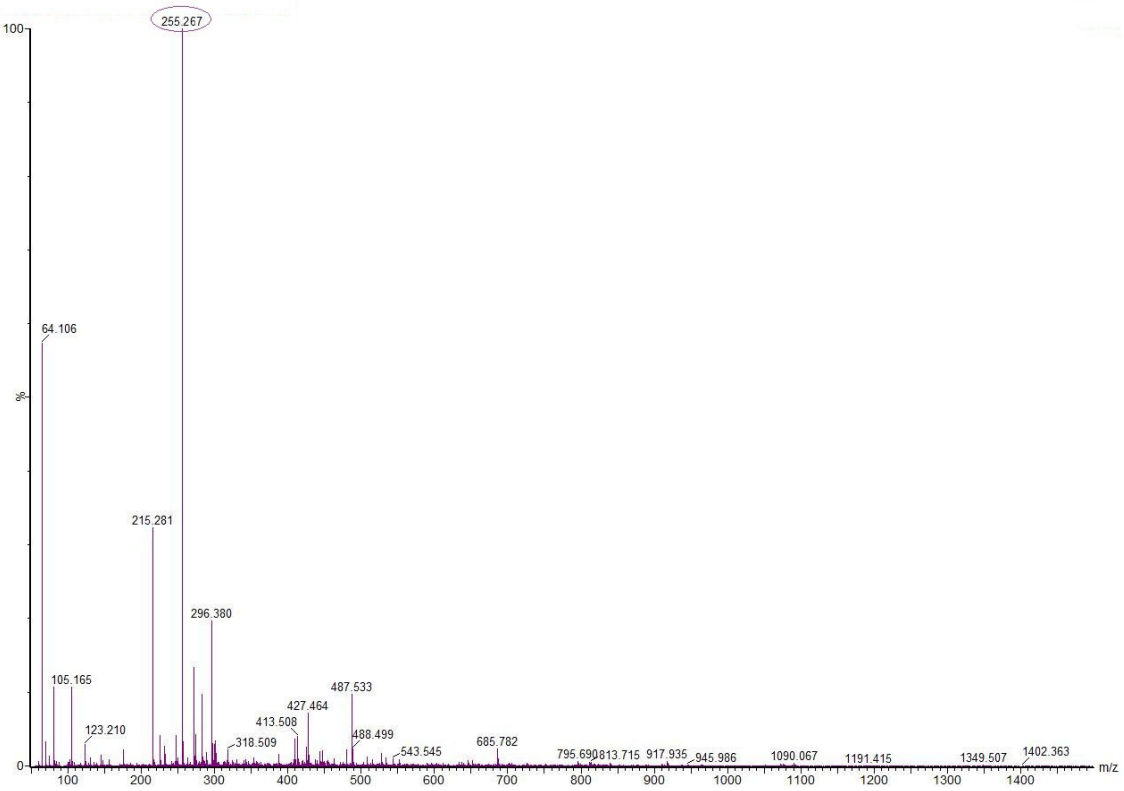


- As a reference for characterization data of 2,3,4,5-Di-isopropylidene-D-xylitol can be referred and compared also with reference **[35].** A.R. Rufino, F.C. Biaggio, J.C. Santos, H.F. de Castro, *Journal of chemical technology and biotechnology*, **2009**, *84*, 957-960.

FT-IR (ν): 3445, 2962, 2858, 1465, 1460, 1383, 1375, 1215, 1125, 1003.



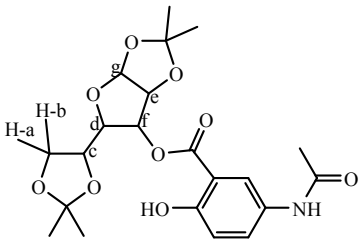
MS: HRMS $(M+Na)^+$, m/z 255.267 [calcd; 232.131, formula ($C_{11}H_{20}O_5$)].

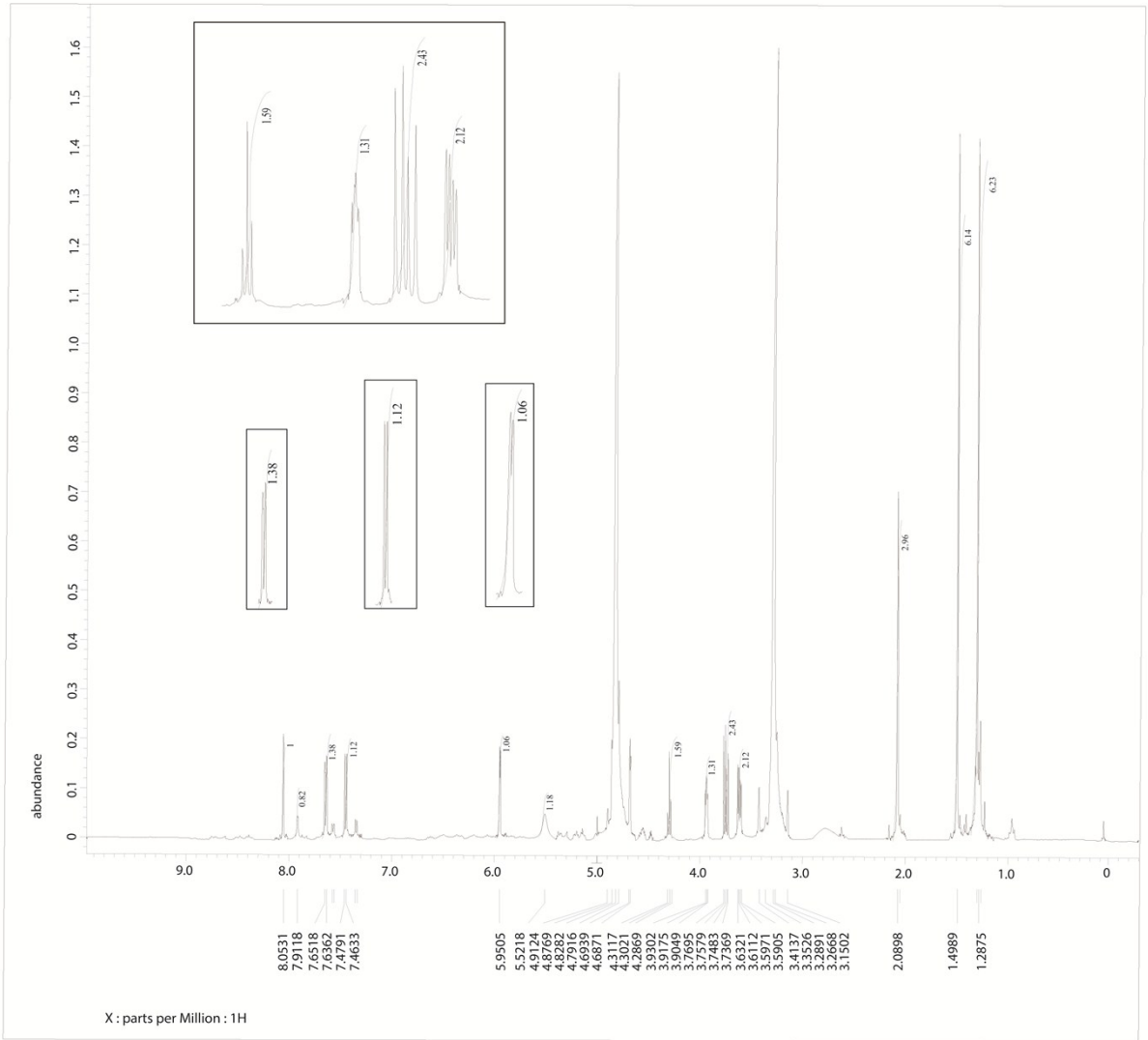


2.4. 3-*O*-*N*-acetyl-5-aminosalicylate-1,2:5,6-Di-*O*-isopropylidene-D-glucfuranose (d)

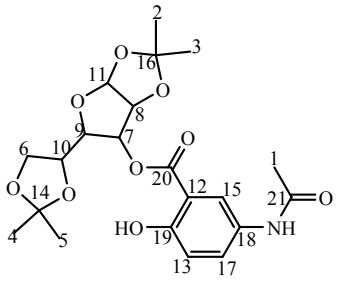
Yield: 57%. M.p: 182-185°C. Light gray crystals.

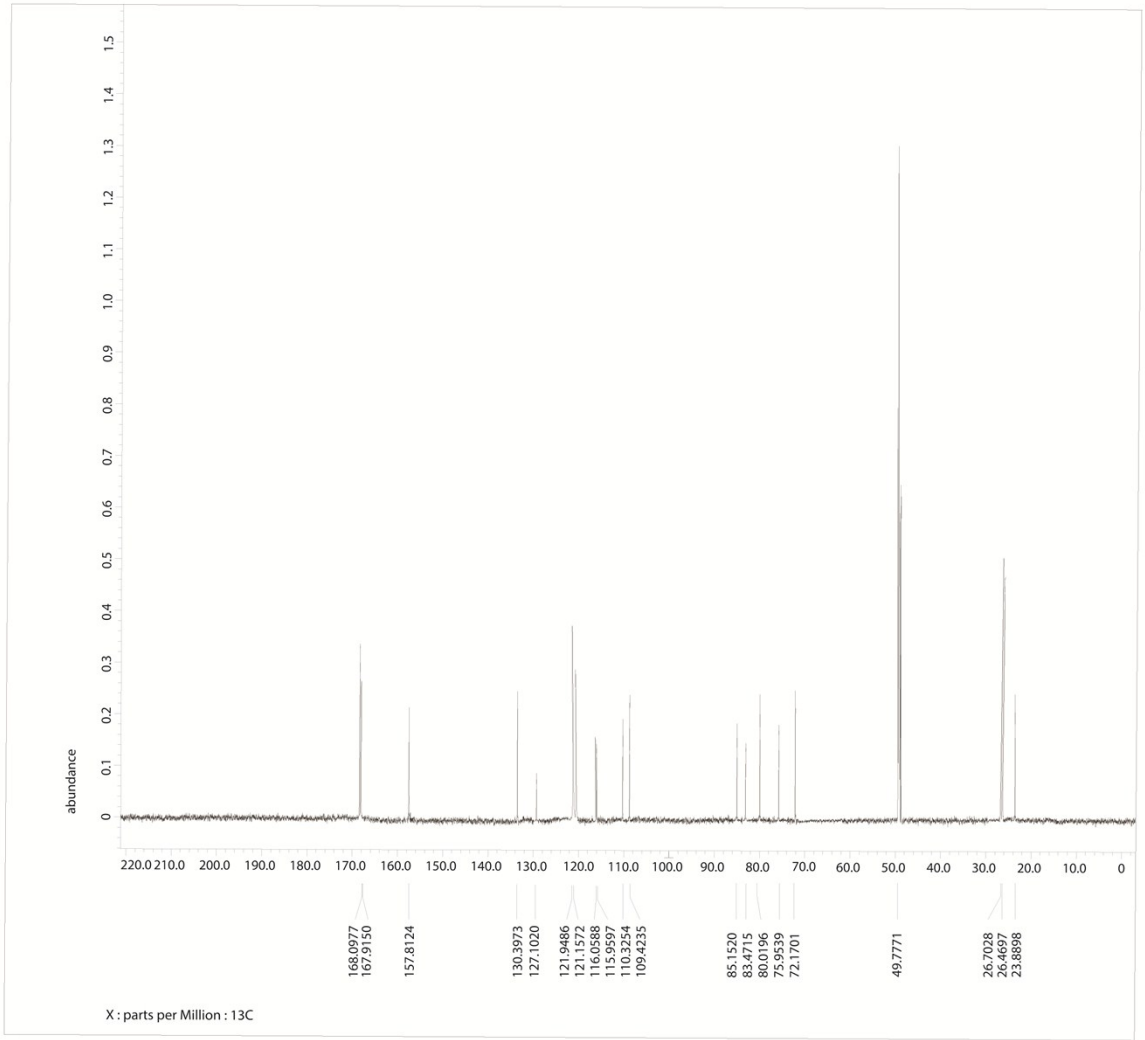
^{1}H NMR (500 MHz, methanol-d_4): δ (ppm) = 1.28 (6H, bs, 3 each, 2 × CH_3), 1.49 (6H, s, 3 each, 2 × CH_3), 2.08 (3H, s, O=C-CH_3), 3.59 (2H, dd, *J*= 7.2 Hz, *J*= 3.3 Hz, H-a, H-b), 3.73 (2H, dd, *J*= 10.5 Hz, *J*= 5.7 Hz, H-c, H-d), 3.90 (1H, t, *J*= 6.3 Hz, H-e), 4.28 (1H, t, *J*= 7.6 Hz, H-f), 5.47 (1H, s, Ar-OH), 5.95 (1H, d, *J*= 3.4 Hz, H-g), 7.46 (1H, d, *J*= 7.8 Hz, Ar-CH), 7.63 (1H, d, *J*= 7.9 Hz, 1H, Ar-CH), 7.91 (1H, s, NH), 8.05 (s,1H, Ar-CH).



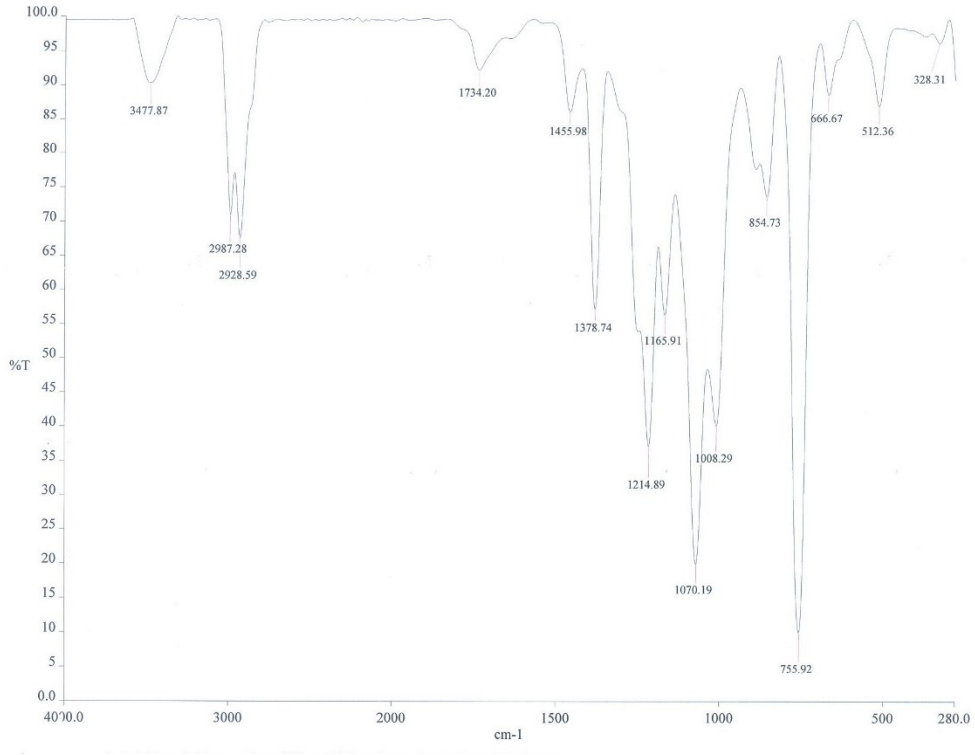


^{13}C NMR (125.8 MHz, methanol-d_4) δ = 23.8 (C-1), 26.4, 26.7; (C-2, C-3, C-4, C-5), 72.1 (C-6), 75.9 (C-7), 80.0 (C-8), 83.4 (C-9), 85.1 (C-10), 109.4 (C-11), 110.3 (C-12), 115.9 (C-13), 116.0 (C-14), 121.1 (C-15), 121.9 (C-16), 127.1 (C-17), 130.3 (C-18), 157.8 (C-19), 167.9 (C-20), 168.0 (C-21).

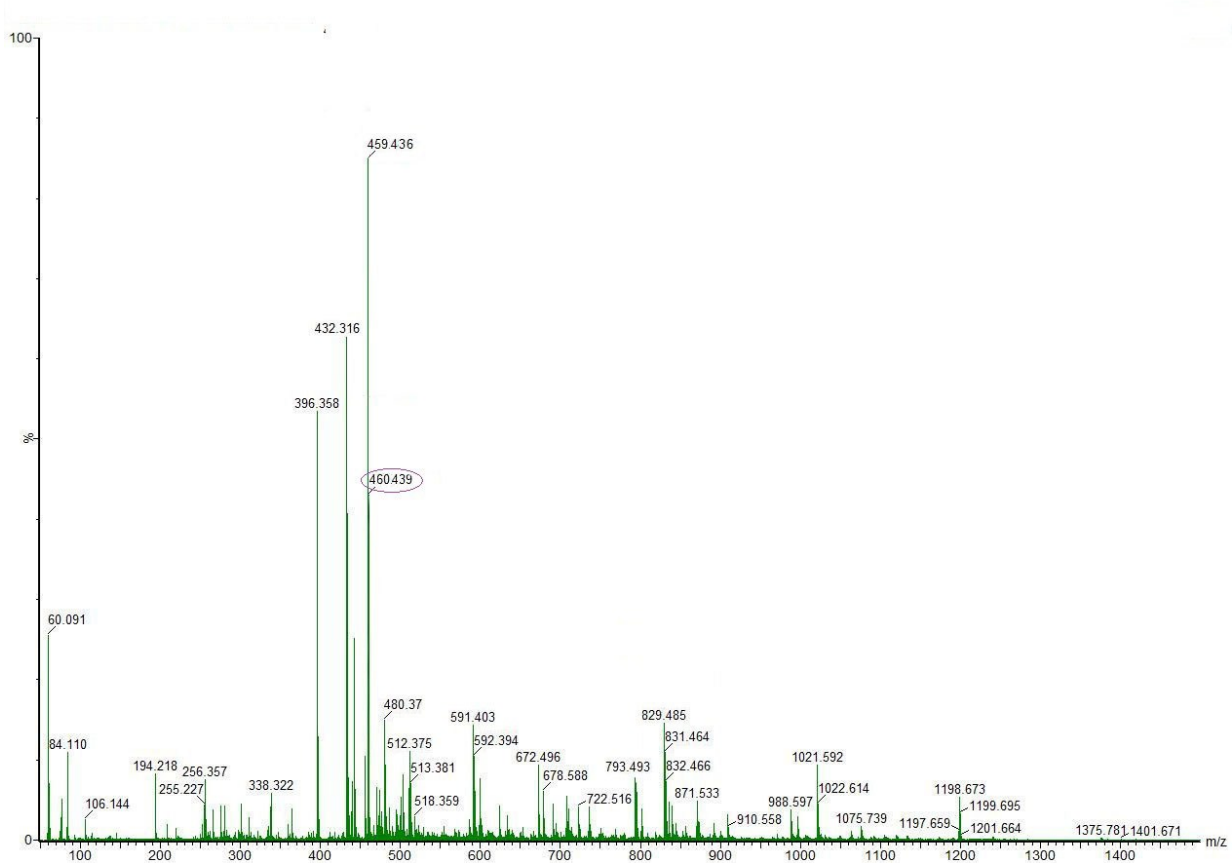




FT-IR (ν): 3477, 2987, 2928, 1734.20, 1455, 1378, 1214, 1165, 1070, 1008.



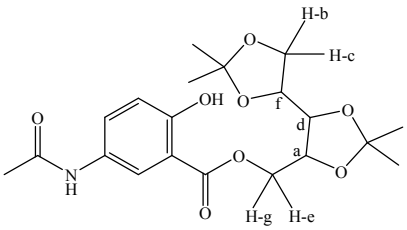
MS: HRMS $(M+Na)^+$, m/z 460.439 [calcd; 437.169, formula ($C_{21}H_{27}NO_9$)].

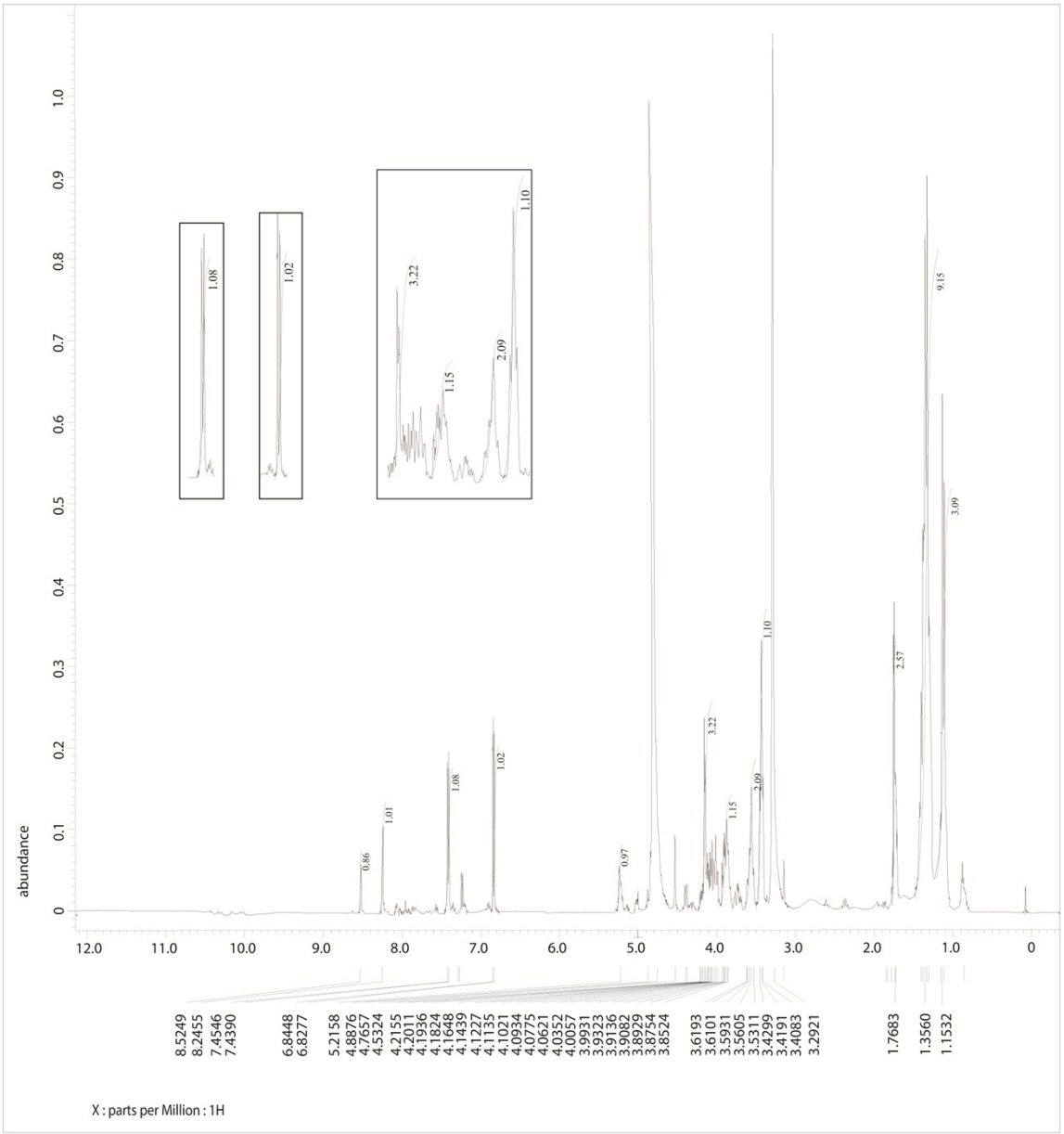


2.5. 1-*O*-*N*-acetyl-5-aminosalicylate-2,3,4,5-Di-isopropylidene-D-xylitol (e)

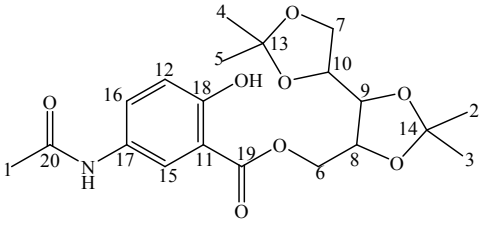
Yield: 47%. M.p: 151-153°C. White crystals.

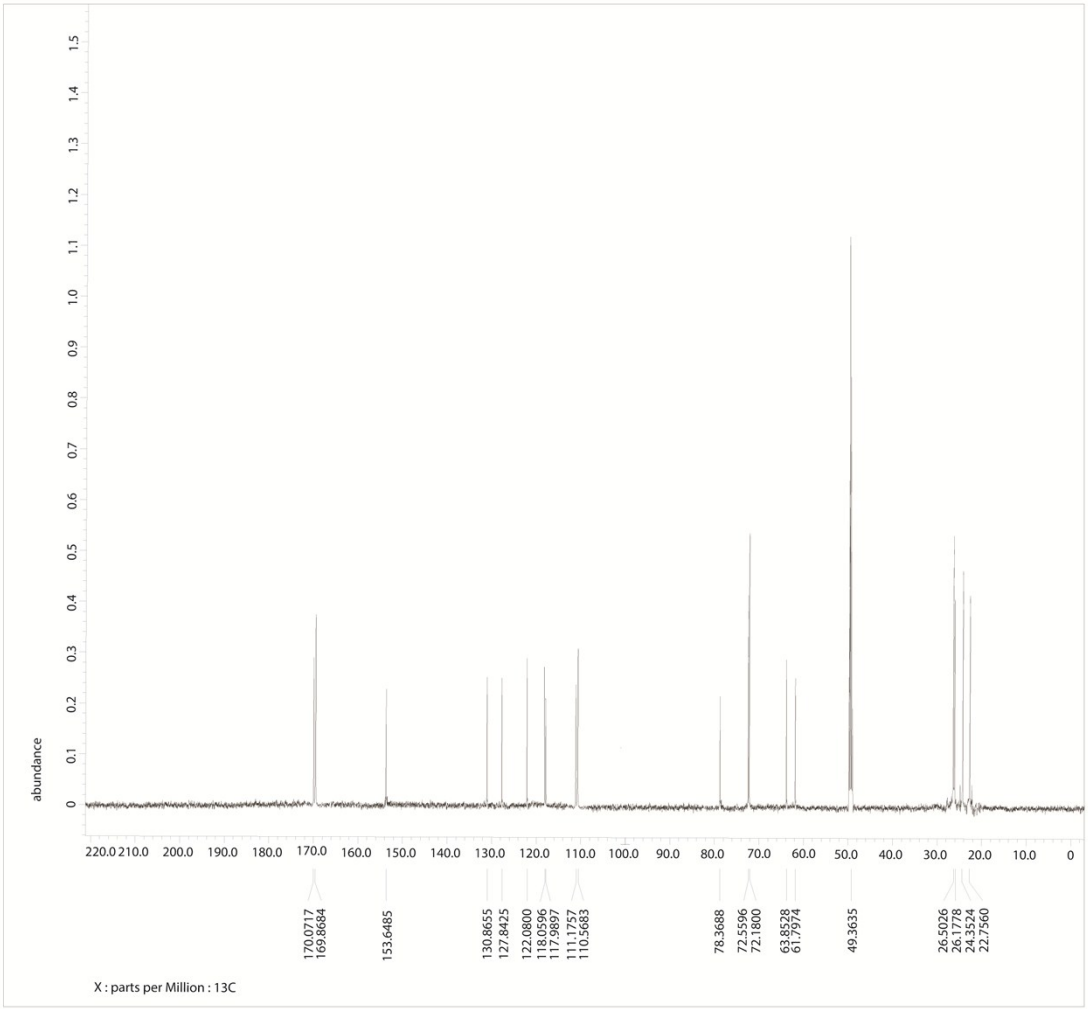
^{1}H NMR (500 MHz, Methanol-d_4): δ (ppm) = 1.15 (3H, brs, CH_3), 1.35 (9H, s, 3 each, 3 × CH_3), 1.76 (3H, s, O=C-CH_3), 3.40 (1H, t, *J* = 5.4 Hz, H-a), 3.56-3.61 (2H, m, H-b, H-c), 3.85-3.93 (1H, m, H-d), 3.99-4.18 (3H, m, H-e, H-f, H-g), 5.21 (1H, s, OH), 6.83 (1H, d, *J* = 8.5 Hz), 7.43 (1H, d, *J* = 7.8 Hz), 8.24 (1H, s, NH), 8.52 (1H, s).



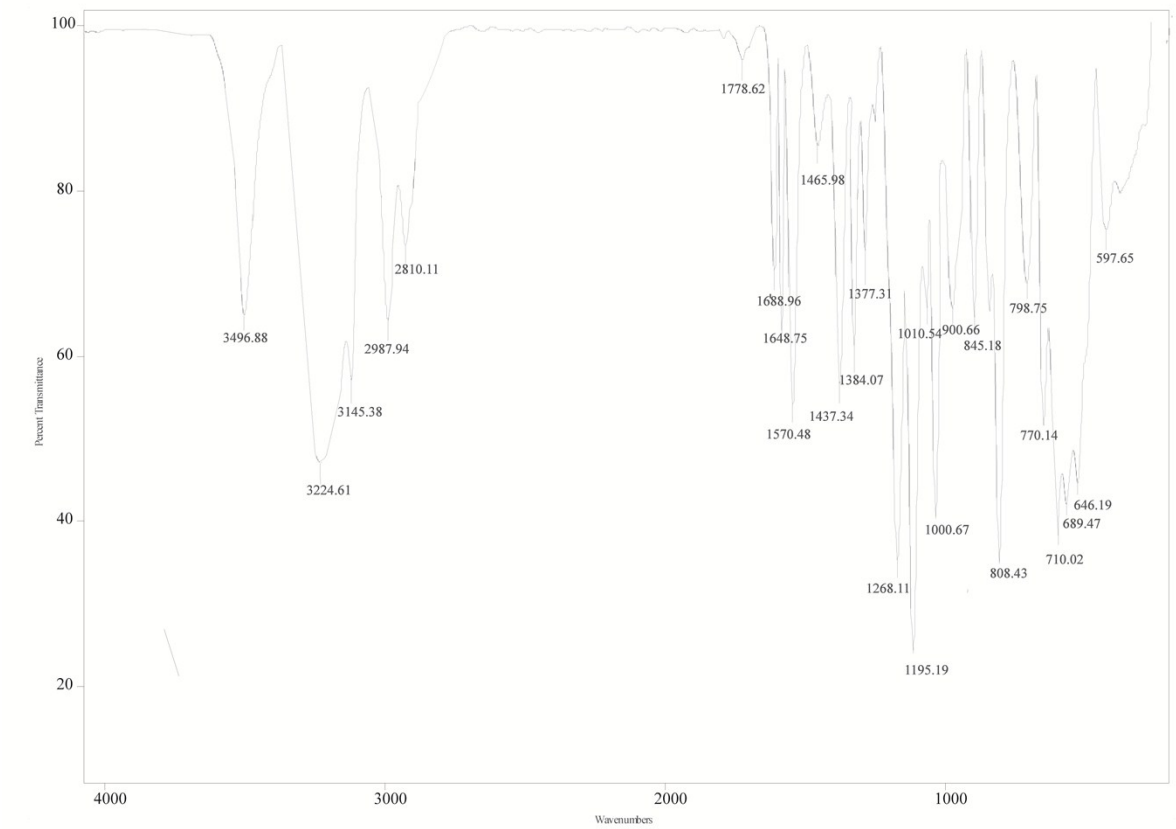


^{13}C NMR (125.8 MHz, methanol-d_4) δ = 22.7 (C-1) , 24.3, 26.1, 26.5; (C-2, C-3, C-4, C-5) 61.7 (C-6), 63.8 (C-7), 72.1 (C-8), 72.5 (C-9), 78.3 (C-10), 110.5 (C-11), 111.1 (C-12), 117.9 (C-13), 118.0 (C-14), 122.0 (C-15), 127.8 (C-16), 130.8 (C-17), 153.6 (C-18), 169.8 (C-19), 170.0 (C-20).

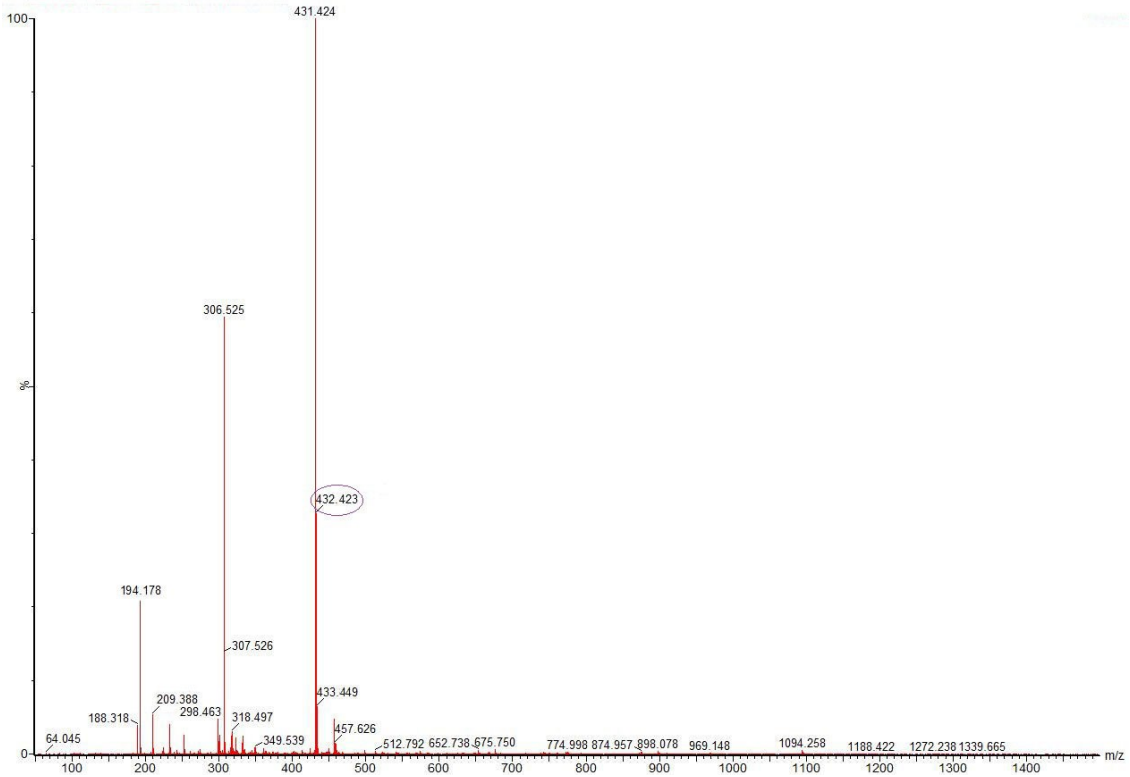




FT-IR (ν): 3496, 3224, 3145, 2987, 2810, 1778, 1688, 1648, 1570, 1465, 1437, 1384, 1377, 1268, 1195, 1010, 1000.



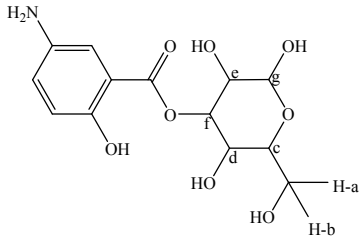
MS: HRMS $(M+Na)^+$, m/z 432.423 [calcd; 409.174, formula ($C_{20}H_{27}NO_8$)].

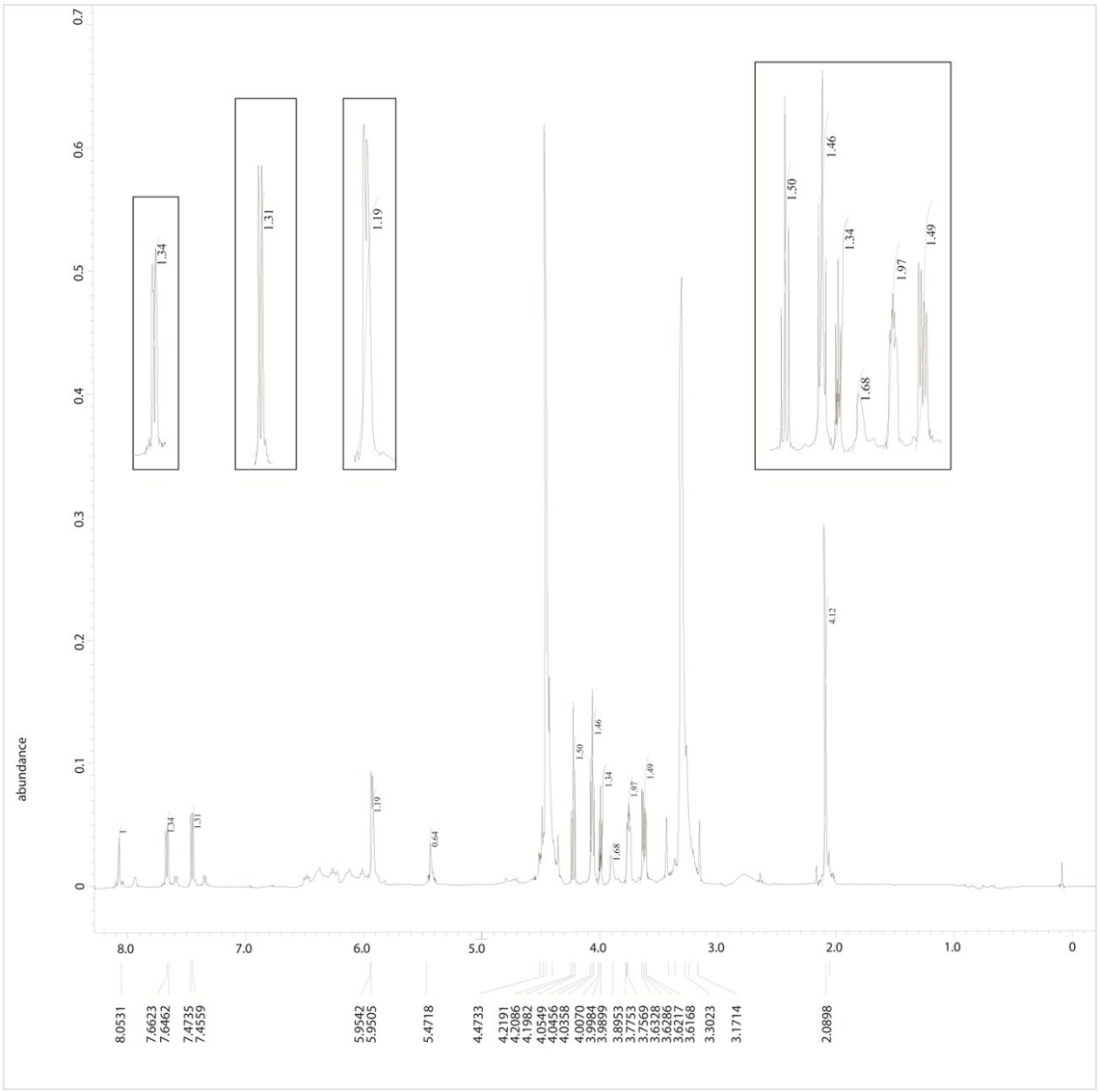


2.6. 3-*O*-5-aminosalicylate-*D*-glucopyranoside (f)

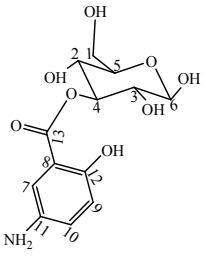
Yield: 41%. M.p: 191-193°C. White crystals.

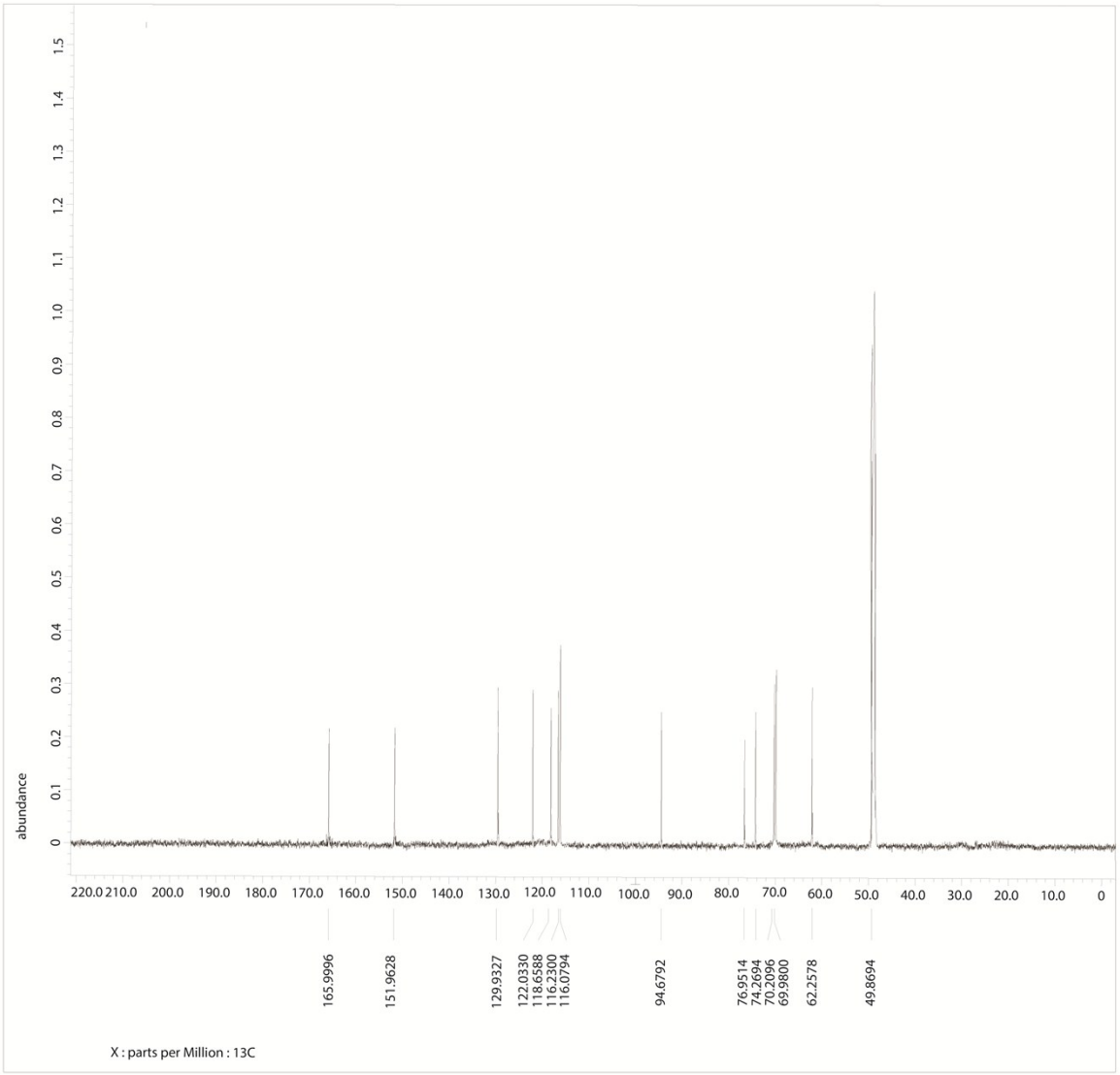
^{1}H NMR (500 MHz, methanol-d_4): δ(ppm) = 2.08 (4H, s, 4×OH), 3.61 (1H, dd, *J*= 5.8 Hz, *J*= 2.2 Hz, H-a), 3.75-3.77 (2H, m, H-b, H-c), 3.89 (2H, s, NH_2), 3.99 (1H, t, *J*= 4.2 Hz, H-d), 4.03 (1H, t, *J*= 4.9 Hz, H-e), 4.20 (1H, t, *J*= 5.2 Hz, H-f), 5.47 (1H, s, Ar-OH), 5.95 (1H, d, *J*= 1.8 Hz, H-g), 7.45 (1H, d, *J*= 8.8 Hz, Ar-CH), 7.64 (1H, d, *J*= 7.9 Hz, Ar-CH), 8.05 (1H, s, Ar-CH).



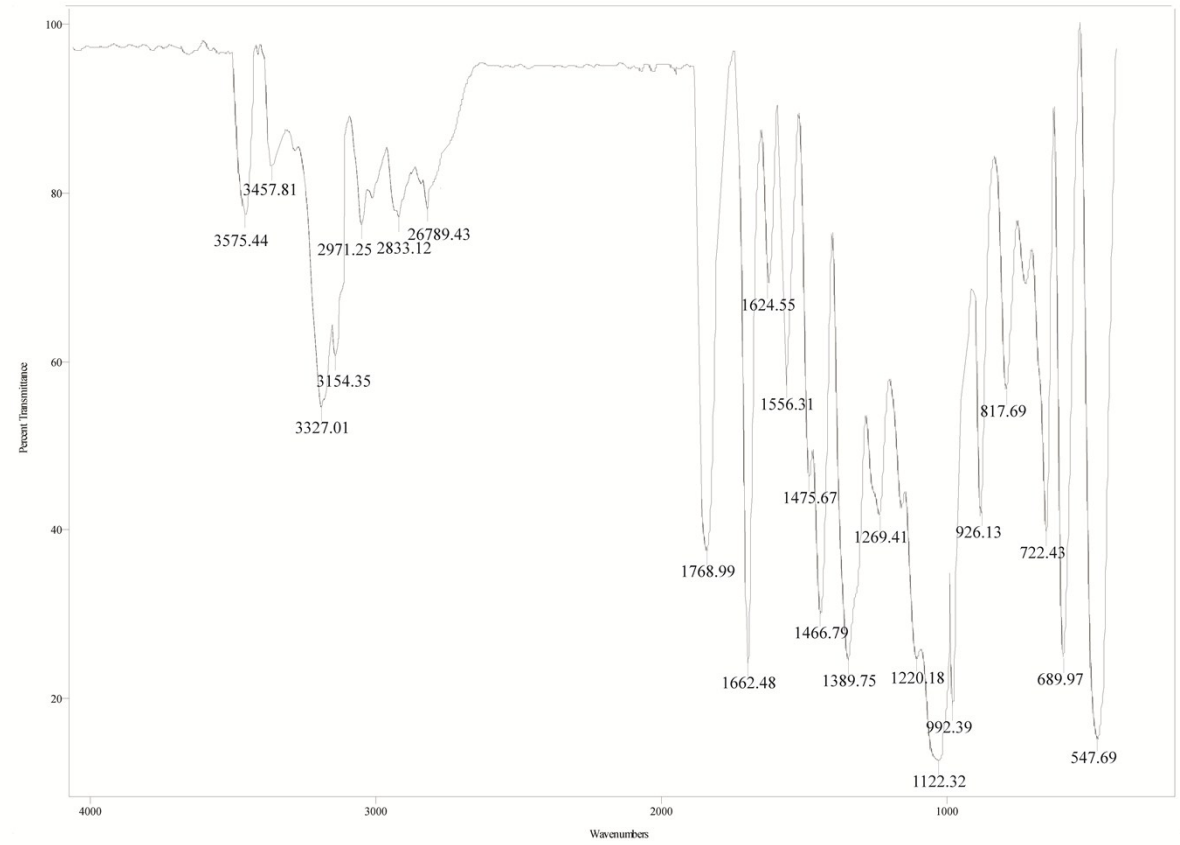


^{13}C NMR (125.8 MHz, methanol-d_4) δ (ppm) = 62.2 (C-1), 69.9 (C-2), 70.2 (C-3), 74.2 (C-4), 76.9 (C-5), 94.6 (C-6), 116.0 (C-7), 116.2 (C-8), 118.6 (C-9), 122.0 (C-10), 129.9 (C-11), 151.9 (C-12), 165.9 (C-13).

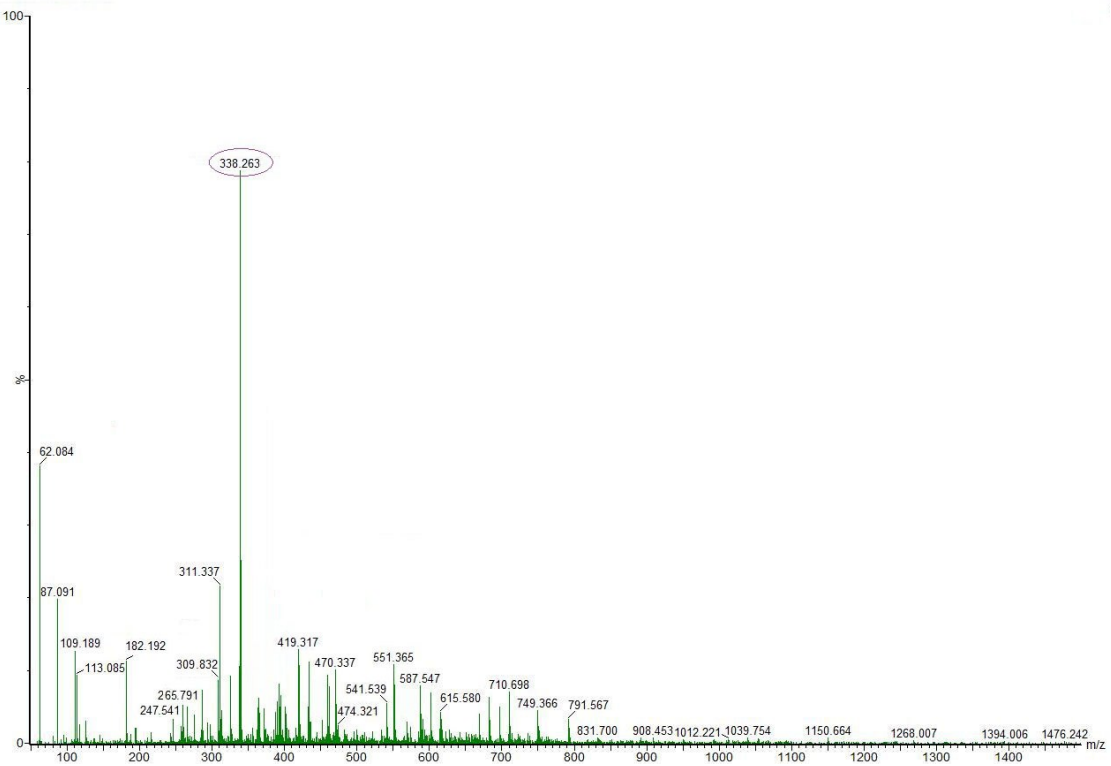




FT-IR (ν): 3575, 3475, 3327, 3154, 2971, 2833, 2689, 1768, 1768, 1662, 1624, 1556, 1475, 1269, 1220, 1122.



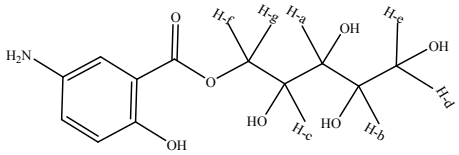
MS: HRMS $(M+Na)^+$, m/z 338.263 [calcd; 315.095, formula ($C_{13}H_{17}NO_8$)].

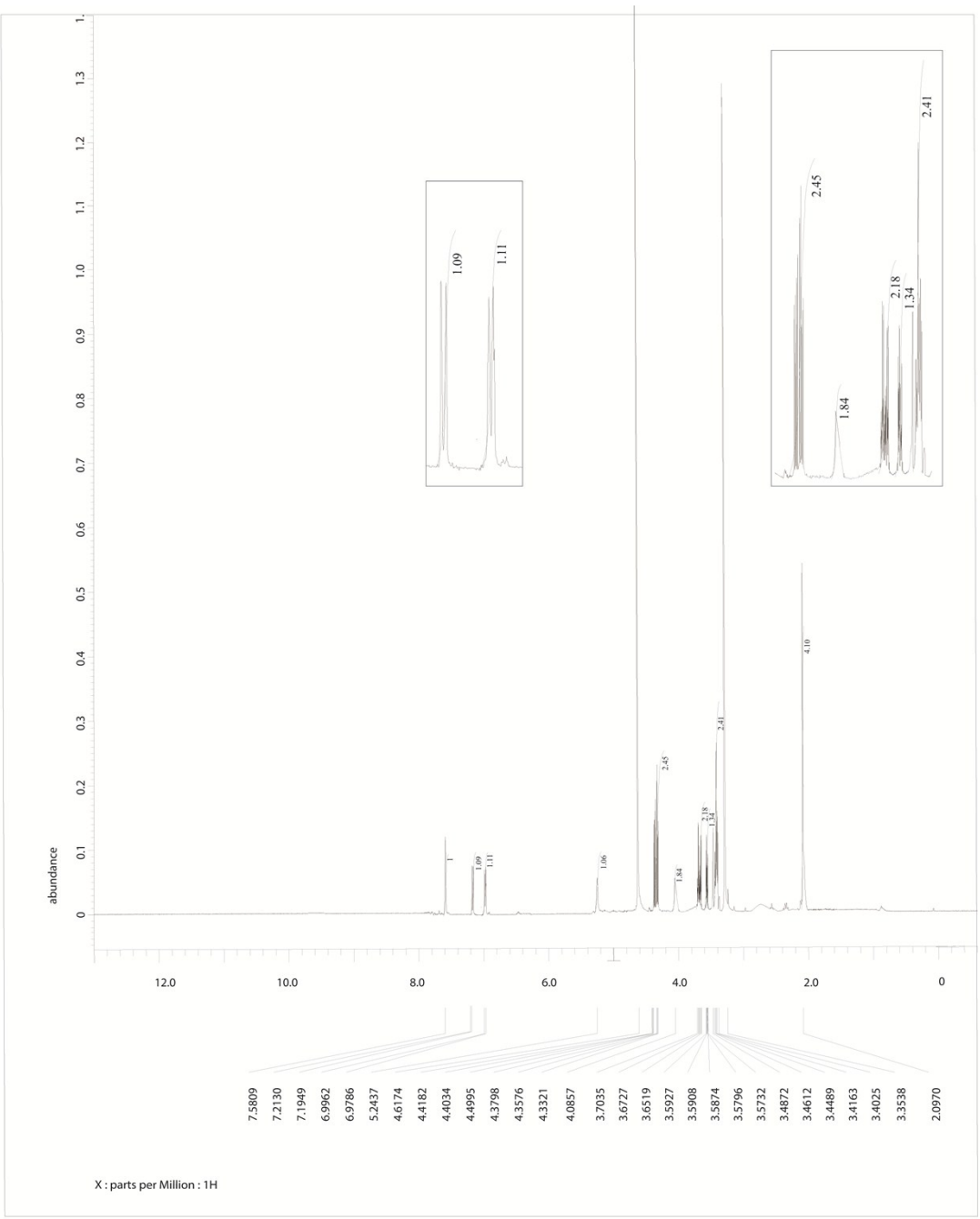


2.7. 1-*O*-5-aminosalicylate-*D*-xylitol (g)

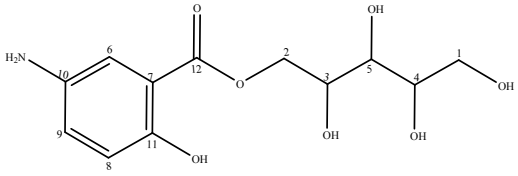
Yield: 38%. M.p: 164-166°C. White crystals.

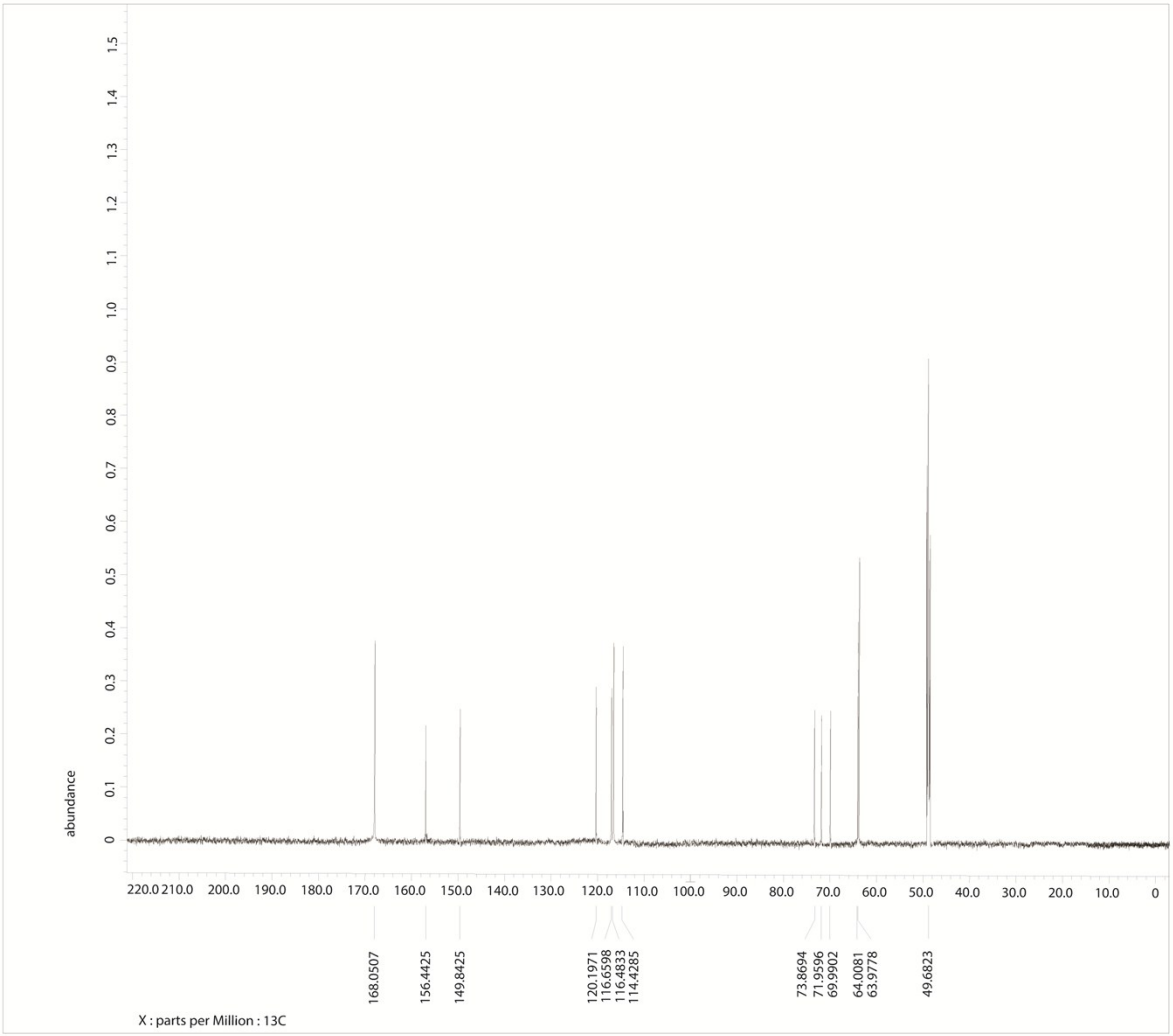
^{1}H NMR (500 MHz, methanol-d_4): δ = 2.09 (4H, s, 4 × OH), 3.40-3.46 (2H, m, H-a, H-b), 3.57-3.59 (1H, m, H-c), 3.65-3.70 (2H, m, H-d, H-e), 4.08 (2H, s, NH_2), 4.33-4.41(2H, m, H-f, H-g), 5.28 (1H, s, Ar-OH), 6.97 (1H, d, *J*=8.8 Hz, Ar-CH), 7.19 (1H, d, *J*=9.0 Hz, Ar-CH), 7.58 (1H, s, Ar-CH).



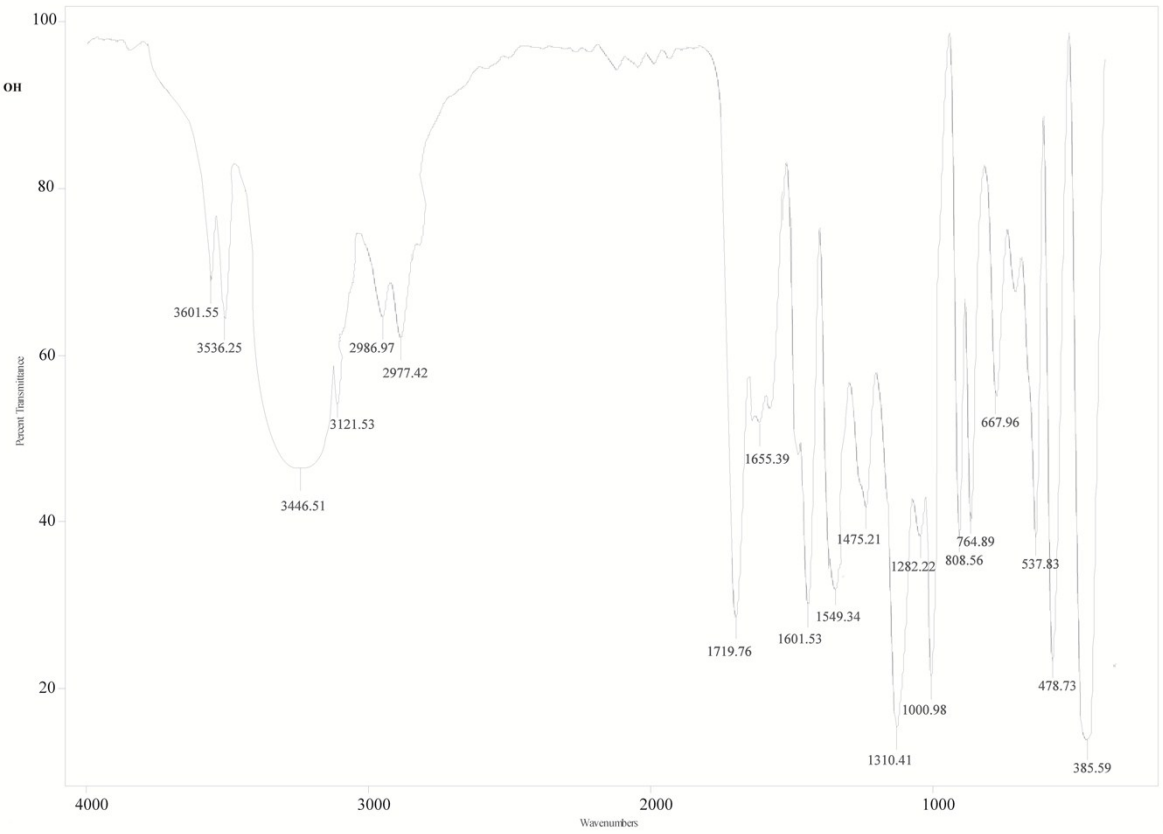


^{13}C NMR (125.8 MHz, methanol-d_4) δ = 63.9 (C-1), 64.0 (C-2), 69.9 (C-3), 71.9 (C-4), 73.8 (C-5), 114.4 (C-6), 116.4 (C-7), 116.6 (C-8), 120.1 (C-9), 149.6 (C-10), 156.4 (C-11), 168.0 (C-12).

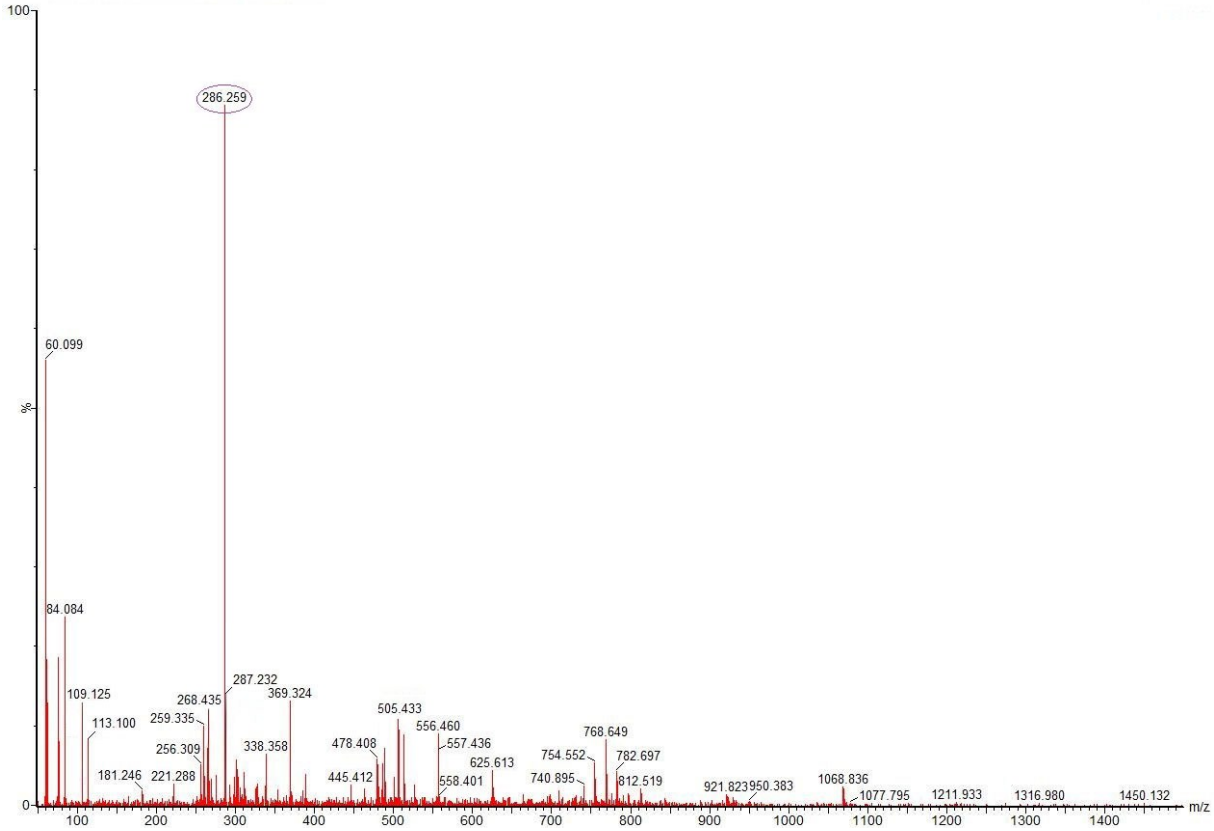




FT-IR (ν): 3601, 3536, 3446, 3121, 2986, 2977, 1719, 1601, 1549, 1475, 1310, 1282, 1000.



MS: HRMS $(M-H)^-$, m/z 286.259 [calcd; 287.101, formula ($C_{12}H_{17}NO_7$)].



3. Image of petri plate in anti- bacterial test via disk diffusion method

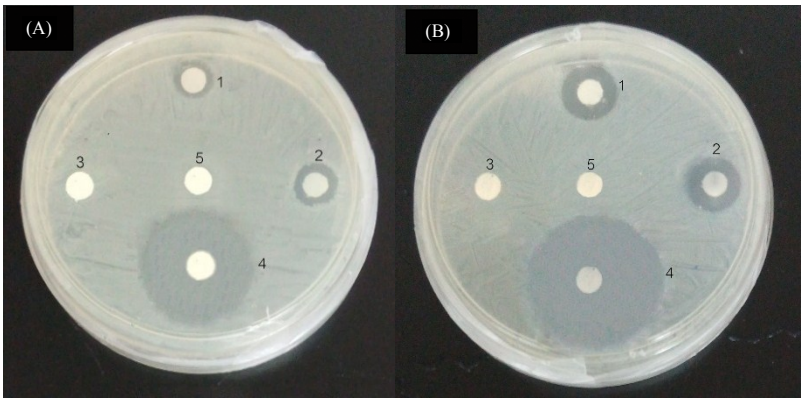


Fig 1. Showing the antibacterial activity results of samples against (A): *Escherichia coli* and (B) *Staphylococcus aureus* bacteria. No 1: **f**, No 2: **g**, No 3: 5-ASA, No 4: positive control (streptomycin), No 5: negative control (ethanol).

4. Molecular Docking analysis

4.1. Molecular Docking study into COX-1 protein

In docking study toward COX-1 protein the co-crystallized ibuprofen was utilized as a positive control ligand. The key amino acids of COX-1 consist: His90, Arg120, Val349, Tyr355, Arg53, Met522 and Glu524 [1, 2] where carboxylic group of ibuprofen formed two hydrogen bonds between NH and NH_2 groups of Arg120 and one hydrogen bond between phenolic OH of Ty355. As cited in the literatures [2, 3], if the RMSD (root mean square deviation) of the best docked conformation of co-crystal ligand is ≤ 2 Å from the experimental one the used scoring function is reliable. The RMSD of 0.98Å for ibuprofen validated the accuracy of the AutoDock4.2 performance. 5-ASA exhibited two hydrogen bonds with NH and NH_2 groups of Arg120 and one hydrogen bond with phenolic OH of Ty355 from its carboxyl group. Two hydrogen bonds were observed between OH-C_4 from **f** with Val349 and Ser353 carboxyl and amine groups, respectively. Also, **f** showed two more hydrogen bonds with Arg120 and Ser530. **g** conserved three hydrogen bonds between its OH-C_5, amine and phenolic hydroxyl groups with Arg120, Met522 and Ser530, respectively. In addition, the binding energy of the new products was moderate in comparison with ibuprofen (ΔG: -8.42 kcal/mol), however, compounds **f** (ΔG: -5.78 kcal/mol) revealed greater binding energy toward both **g** (ΔG: -4.22 kcal/mol) and 5-ASA (ΔG: -4.33 kcal/mol) which exhibited almost the equal binding energies to each other, (Table 1 and Fig 2).

Table 1. The docking results (AutoDock 4.2), regarding the binding free energy: [ΔG (kcal/mol)], distances and hydrogen bonds between compounds and amino acids involved in COX-1

Entry	Compound name	ΔG (kcal/mol)	Hydrogen bonds between atoms of compounds and amino acids into COX-1		
			Atom of compound	Amino acid	Distance (Å)
1	**Ibuprofen**	-8.42	COO	Ty355 (p-OH)	2.59
			COO	Arg120 (NH2, NH)	2.61, 2.69
2	**5-ASA**	-4.33	COO	Ty355 (p-OH)	2.59
			COO	Arg120 (NH2, NH)	2.61, 3.03
3	**f**	-5.78	p-OH	Ser530 (COO)	2.62
			C_6-OH	Arg120 (NH)	3.12
			C_4-OH	Val349 (COO)	3.02
			C_4-OH	Ser353 (NH_2)	2.90
5	**g**	-4.22	NH2	Met522 (COO)	2.71
			C_5-OH	Arg120 (NH)	2.94
			p-OH	Ser530 (COO)	2.90

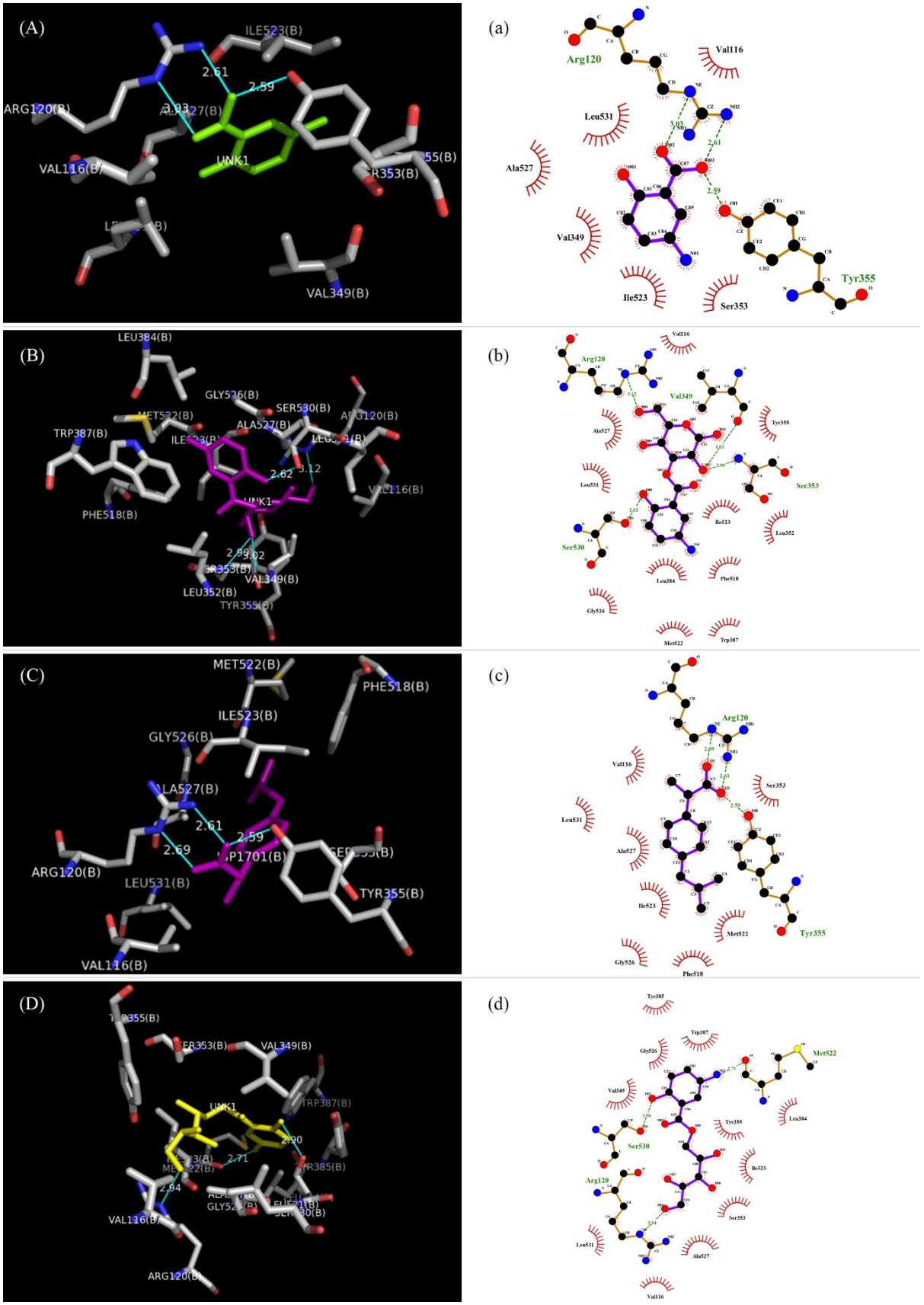


Fig 2. Showing images visualized by Pymol (capital letter) and Ligplot (small letter) program for the samples docked into COX-1 in the best of their conformation into the binding site. (A & a): 5-ASA (green), (B & b): **f** (purple), (C & c): Ibuprofen (purple), (D & d): **g** (yellow).

4.2. Molecular Docking study into COX-2 protein

The co-crystallized S58, was used to parameterize molecular docking study against COX-2. The main amino acids in this interaction include: Val349, Ser530, Leu352, Tyr385, Tyr348, Trp387, Gly526, Ala527, Met522, Leu384, His90, Arg120, Tyr355, Arg53, Phe518 and Gly526, where S58 formed four hydrogen bonds with His90, Arg120, Leu352 and Gln192 [1, 2]. The RMSD value of 1.57Å was obtained for docked S58. 5-ASA conserved two hydrogen bonds between carboxyl of Ala527 and phenolic OH of Ty355 with its amine and carboxylic acid groups, respectively. **f** exhibited five hydrogen bonds with the related amino acids in active site of COX-2 protein with Met522, Try385, Arg120 and Try355. Similarly, **g** formed five hydrogen bonds with Tyr385, Val523, Arg120, and Try355. Although the binding energies of the new derivatives were not comparable with the co-crystalized S58 (ΔG: -10.85 kcal/mol), both new compounds became involved in three more hydrogen bonds with amino acids in active site of COX-2 protein than 5-ASA. Additionally, based on binding affinities **f** (ΔG: -5.78 kcal/mol) seems to be a more reasonable candidate than **g** (ΔG: -4.12 kcal/mol) against COX-2, since **f** showed almost one and half fold greater binding energy than the parent drug (ΔG: -3.49 kcal/mol), (Table 2 and Fig 3).

Table 2. The docking results (AutoDock 4.2), regarding the binding free energy: [ΔG (kcal/mol)], distances and hydrogen bonds between compounds and amino acids involved in COX-2

Entry	Compound name	ΔG (kcal/mol)	Hydrogen bonds between atoms of compounds and amino acids into COX-2		
			Atom of compound	Amino acid	Distance (Å)
1	**S58**	-10.85	F	Arg120 (NH2)	3.20
			S=O	His90 (N)	2.79
			NH_2	Leu352 (COO)	2.76
			NH_2	Gln192(COO)	2.89
2	**5-ASA**	-3.94	NH_2	Ala527 (COO)	2.95
			COO	Tyr355 (p-OH)	2.93
3	**f**	-5.78	p-OH	Ty385 (p-OH)	2.80
			NH_2	Met522 (COO)	2.93
			C_1-OH	Tyr355 (p-OH)	2.62
			C_6-OH	Arg120 (NH)	3.11
			C-O-C	Arg120 (NH)	3.01
4	**g**	-4.07	p-OH	Val523 (COO)	2.58
			NH_2	Ty385 (p-OH)	2.77
			C_4-OH	Arg120 (NH)	2.96
			C_3-OH	Arg120 (NH)	2.71
			C_3-OH	Ty355 (p-OH)	2.93

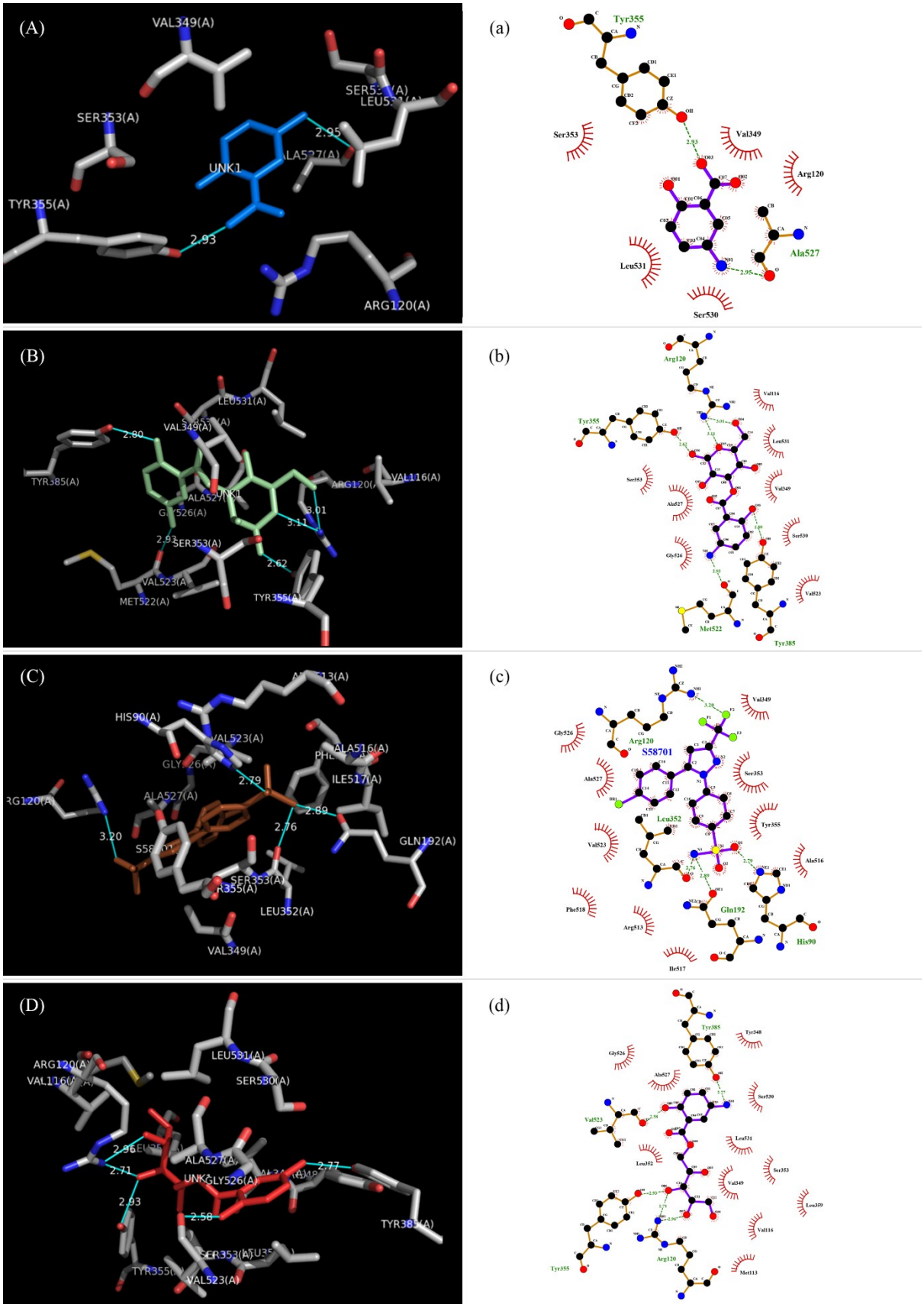


Fig 3. Showing images visualized by Pymol (capital letter) and Ligplot (small letter) program for the samples docked into COX-2 in the best of their conformation into the binding site. (A & a): 5-ASA (blue), (B & b): **f** (light green), (C & c): S58 (brown), (D & d): **g** (red).

4.3. Molecular Docking study into 5-LOX protein

It has been found that the active site of 5-LOX is around catalyst non-hem iron atom. The iron is coordinated by three conserved histidines (histidines 367, 372, and 550), as well as the main-chain carboxylate of the C terminus (Ile673). The other predominantly involved amino acids contain: Tyr181, Ala603, Ala606, His600 and Thr364 [4]. As regards, there is no reference co-crystalized ligand into 5-LOX, the same parameters applied in docking against COX-1 and COX-2 were utilized. Additionally, hydrogen bond interactions between the samples and the amino acids in active site confirmed that docking carried out in the targeted site. 5-ASA formed one hydrogen bond from its amine group with carboxyl group of Ala606. Two hydrogen bindings were occurred between OH- C_6 and OH-C_5 of **f** with phenolic OH of Tyr181. Three more hydrogen bonds formed between phenolic OH and OH groups of C_2 and C_1 with Ile673, His367 and Gln363, respectively. **g** conserved two hydrogen bonds from its amine group with carboxyl group of Ile406 and carbonyl group of Asn407. Besides, OH-C_3 and OH-C_4 exhibited two hydrogen bonds with carboxyl groups of Gln363. One more hydrogen bond observed between OH-C_5 of **g** and OH-CH of Thr364. Studying of binding energy of the new derivatives predicted both **f** (ΔG: -5.40 kcal/mol) and **g** (ΔG: -4.55 kcal/mol) have stronger binding affinities than 5-ASA (ΔG: -3.68 kcal/mol) and may be potential candidates against 5-LOX, (Table 4, Fig 4 and Fig 5).

Table 4. The docking results (AutoDock 4.2), regarding the binding free energy: [ΔG (kcal/mol)], distances and hydrogen bonds between compounds and amino acids involved in 5-LOX

Entry	Compound name	ΔG (Kcal/mol)	Hydrogen bonds between atoms of compounds and amino acids into 5-LOX		
			Atom of compound	Amino acid	Distance (Å)
1	**5-ASA**	-3.68	NH_2	Ala606 (COO)	2.48
			p-OH	Ile673 (COO)	2.71
			C_1-OH	Gln363 (COO)	2.72
2	**f**	-5.40	C_2-OH	His367 (N)	2.83
			C_5-OH	Tyr181 (p-OH)	2.97
			C_6-OH	Tyr181 (p-OH)	2.63
			NH_2	Ile406 (COO)	3.00
			NH_2	Asn407 (H_2N-C=O)	3.03
3	**g**	-4.55	C_3-OH	Gln363 (COO)	2.53
			C_4-OH	Gln363 (COO)	2.74
			C_5-OH	Thr364 (HC-OH)	2.64

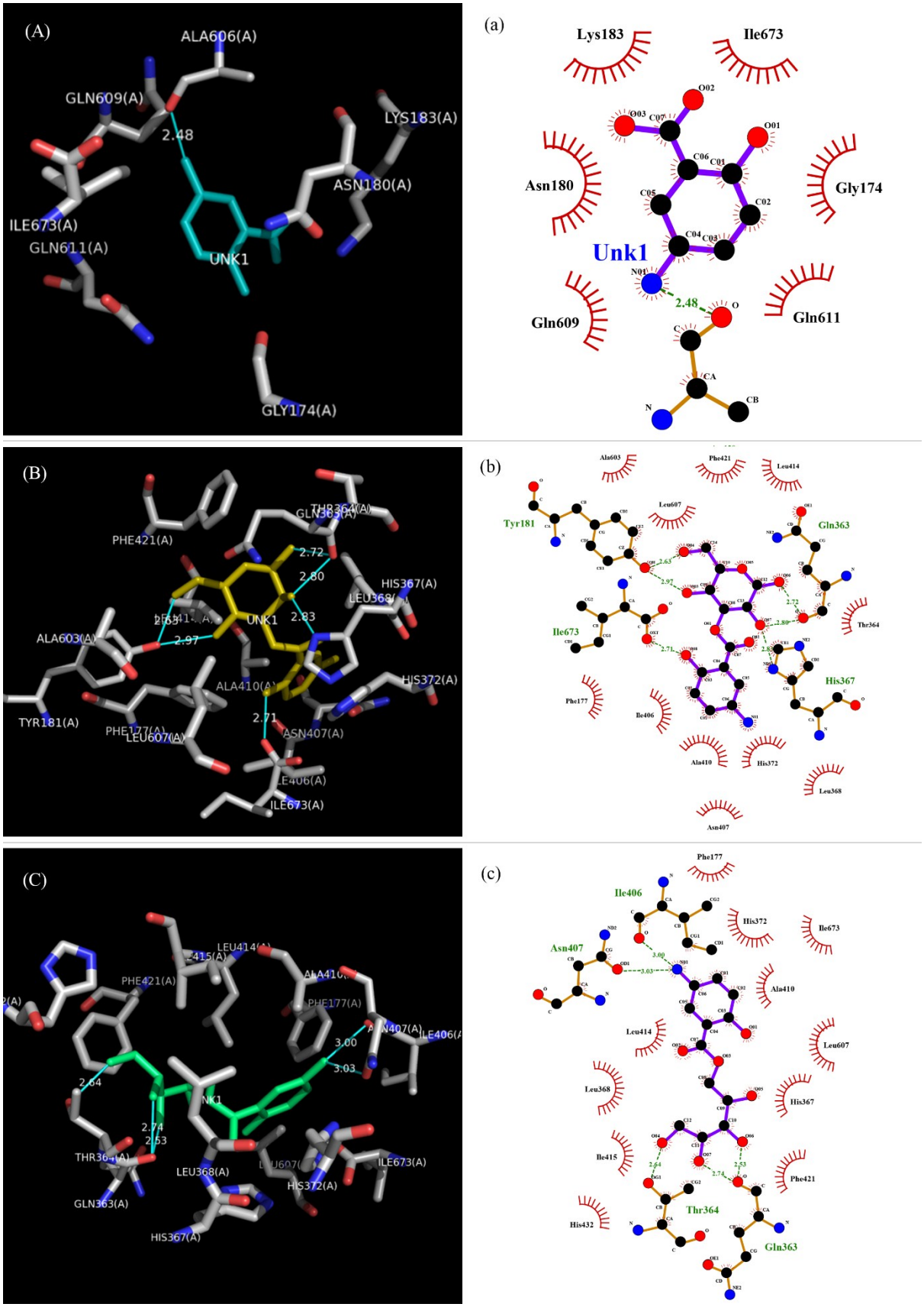


Fig 4. Showing images visualized by Pymol (capital letter) and Ligplot (small letter) program for the samples docked into 5-LOX in the best of their conformation into the binding site. (A & a): 5-ASA (blue), (B & b): **f** (yellow), (C & c): **g** (green).

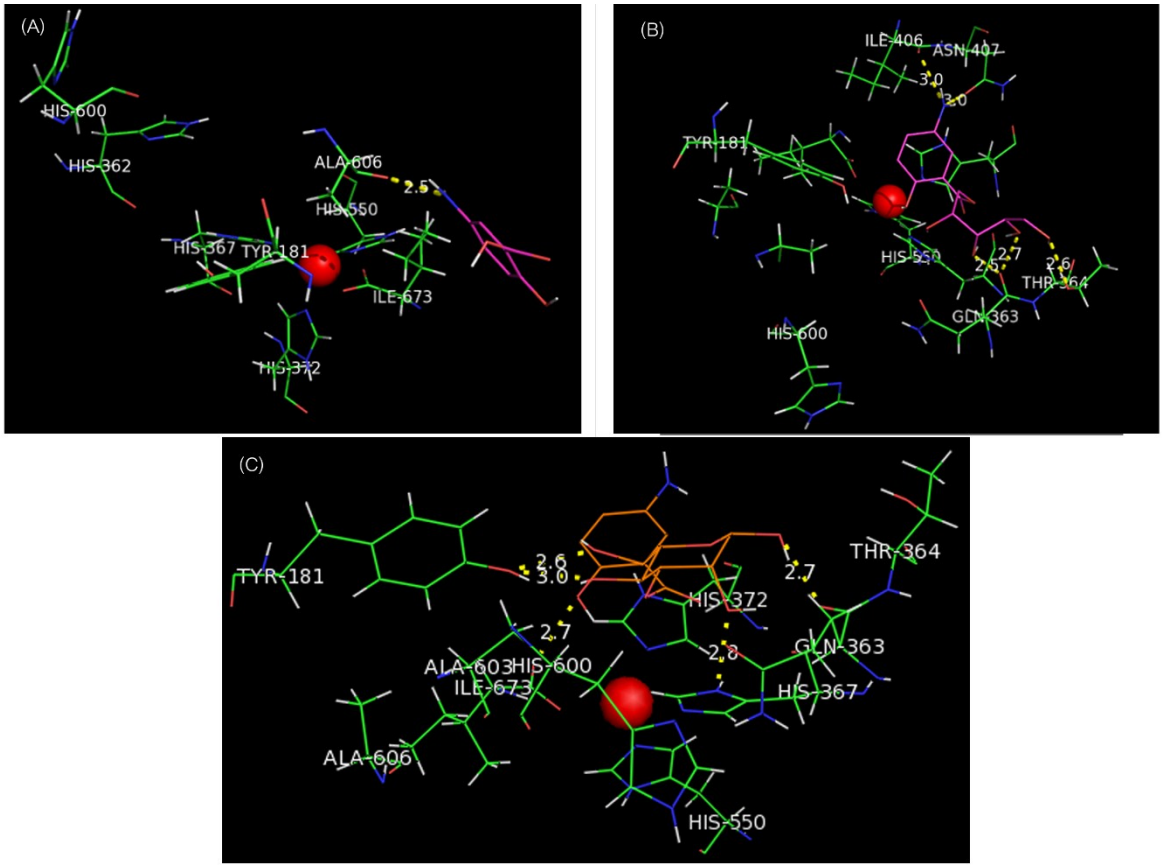
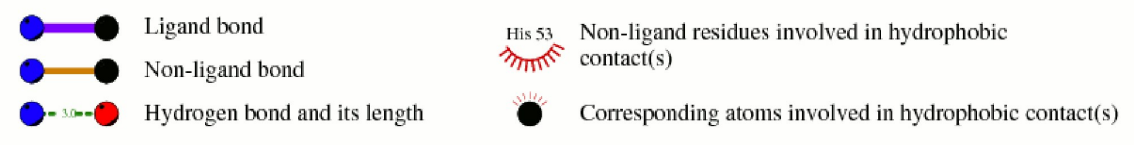


Fig 5. Showing images visualized by Pymol program for the samples docked into 5-LOX in the best of their mode around Iron (red sphere) into the binding site. (A): 5-ASA (pink), (B): **g** (pink), (C): **f** (orange).

Figures related to molecular docking

To understand the possible interactions and predict binding ability of new synthesized compounds with the relevant amino acids in the active site of the protein docking study has been performed into COX-1, COX-2 and 5-LOX enzymes and compared with the parent drug (5-ASA).

The meaning of the items for images taken by ligplot are as follows:



Refrences

[1] M.B. Palkar, A.S. Singhai, P.M. Ronad, A. Vishwanathswamy, T.S. Boreddy, V.P. Veerapur, M.S. Shaikh, R.A. Rane, R. Karpoormath, *Bioorganic & medicinal chemistry*, **2014**, *22*, 2855-2866.
[2] C. Charlier,C. Michaux, *European journal of medicinal chemistry*, **2003**, *38*, 645-659.
[3] G.H. Hegazy,H.I. Ali, *Bioorganic & medicinal chemistry*, **2012**, *20*, 1259-1270.
[4] N.C. Gilbert, S.G. Bartlett, M.T. Waight, D.B. Neau, W.E. Boeglin, A.R. Brash, M.E. Newcomer, *Science*, **2011**, *331*, 217-219.