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Effects of fumarprotocetraric acid, a depsidone from the lichen *Cladonia verticillaris*, on tyrosinase activity

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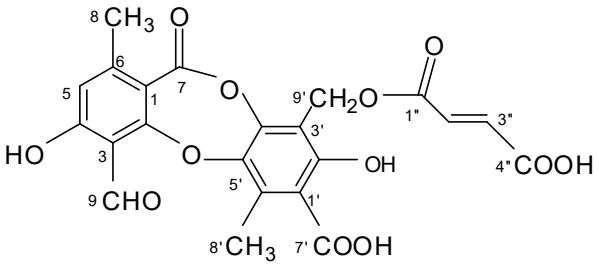
Table 1S. Effect of lichen compounds on enzymes.

Enzyme	Lichen compound and activity
Histidine decarboxylase [13]	Inhibition by lecanoric acid (IC_{50} 3.7 μM).
Prostaglandin synthase [14]	Inhibition (IC_{50}) by 4-*O*-methylcryptochlorophaeic acid (0.34 μM), merochlorophaeic acid (0.43 μM), cryptochlorophaeic acid (2.9 μM), 4,4'-*O*-di-*O*-methylcryptochlorophaeic acid (3.7 μM), boninic acid (3.4 μM), paludosic acid (5.9 μM), ramalinolic acid (7.6 μM), anziaic acid (8.1 μM), 2-*O*-methylsekikaic acid (11.1 μM), 4'-*O*-demethylsekikaic acid (11.9 μM), homosekikaic acid (12.1 μM), sekikaic acid (18.1 μM), sphaerosphorin (25.2 μM), 4'-*O*-methylpaludosic acid (27.4 μM), physodic acid (28.5 μM), β-collatolic acid (33.1 μM), lobaric acid (38.8 μM), α-collatolic acid (41.4 μM), divaricatic acid (42.2 μM), microphyllinic acid (55.5 μM), barbatic acid (66.2 μM), 2,4'-di-*O*-methylnorsekikaic acid (98.1 μM), 2,4-dihydroxy-6-*n*-pentylbenzoic acid (olivetol) (160.0 μM), 2-hydroxy-4-methoxy-6-*n*-pentylbenzoic acid (310.0 μM).
Monoamine oxidase [15,16]	Inhibition (IC_{50}) by norsorolinic acid (0.3 μM), averythrin (3.7 μM), solorinic acid (14.3 μM), emodin (50 μM), averantin (77.9 μM), averantin 6-monomethylether, 4,4'-bissorolinic acid (> 100 μM). Gyrophoric acid and methyl gyrophorate had no effects.
HIV-1 Reverse Transcriptase [17]	Inhibition by protolichesterinic acid (IC_{50} 24.0 μM).
HIV-1 Integrase [9]	Inhibition (3'-processing and strand transfer, respectively) (IC_{50}) by pannarin (2.2 μM and 1.6 μM), stictic acid (4.4 μM and 2.9 μM), virensic acid (4.6 ± 1.6 μM and 6.5 ± 3.9 μM), fumarprotocetraric acid (4.9 ± 2.7 μM and 4.6 ± 2.6 μM), methyl virensate (5.4 ± 1.9 μM and 4.4 ± 0.5 μM), psoromic acid (*syn*. parellic acid), salazinic, physodic, physodic derivative, and norlobaric acids (17.0 μM and 5.3 μM; 19.0 μM and 12.6 μM; 38.5 ± 25.7 μM and 30.9 ± 14.4 μM; 52.2 ± 11.4 μM and 45.7 ± 3.9 μM; 59.9 and 39.2 μM, respectively), atranorin (61.0 μM and 36 μM), usnic acid (126.4 ± 23.5 μM and 123.7 ± 53.4μM), usnic acid derivative *N*-isonicotinoylhydrazone (73.0 μM and 48.5 μM). Atranorin derivatives (Acetyl atranorin, Oxime atranorin, Phenylhidrazone atranorin) were inative. Diffractaic acid was inactive.
5- Lipoxygenase [18,19,20]	Inhibition (IC_{50}) by baeomycesic acid (8.3 μM), tenuiorin (41.6 μM), methyl orsellinate (59.6 μM); lobaric and protolichesterinic acids (ED_{50} 24.5 and 8.4 μg mL^{-1}, respectively).
12(*S*)-lipoxygenase [21]	Inhibition (μM) by lobaric acid (28.5 μM), (+)-protolichesterinic acid (77.0 μM), baeomycesic acid (weak inhibition). (+)-Usnic acid and parietin were not active at the concentrations tested.
RabGGTase [22]	Inhibition by psoromic acid (IC_{50} 1.3 μM).
Prostaglandin E2 synthase-1 [23]	Inhibition (IC_{50}) by perlatolic acid (0.4 μM); physodic acid (0.43 μM); olivetoric acid (1.15 μM); fumarprotocetraric acid, Salazinic acid, variolaric acid, scendin, methyl-β-orcinol carboxylate, evernic acid, and atranorin (>100 μM).

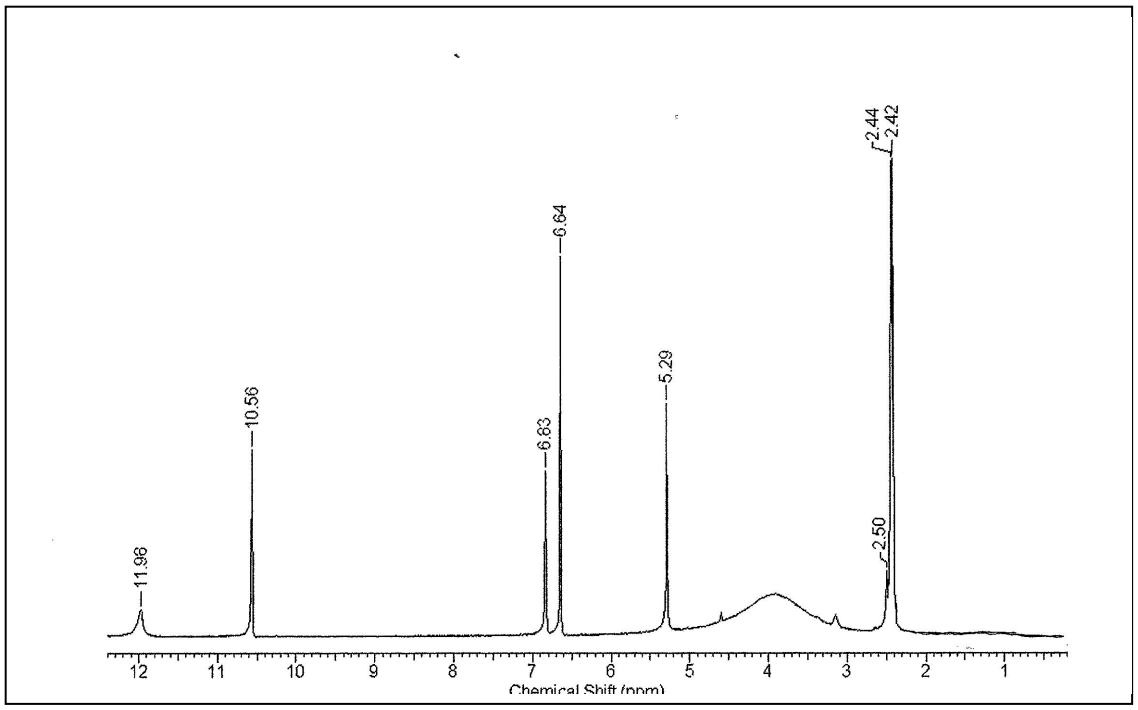
Topoisomerase I (Type IA) [24] (*E. coli* and *Y. pestis*)	Inhibition by anziaic acid (IC_{50} 14-19 μM).
DNA gyrase (Type IIA) [24] (*E. coli*)	Inhibition by anziaic acid (IC_{50} 19 μM).
HumanTopoisomerase I (Type 1B) [24]	Inhibition by anziaic acid (IC_{50} 230 μM).
HumanTopoisomerase IIα (Type IIA) [24]	Inhibition by anziaic acid (IC_{50} 35 μM).
Protein Tyrosine Phosphatase I(Type IB)[25, 26, 27]	Inhibition (IC_{50}) by lobaric acid (0.87 μM), pseudodepsidone 2 (2.48 μM), methyl lobarate (3.02 μM), gyrophoric acid (3.6 μM), pseudodepsidone 1 (6.86 μM), Methyl 2'-*O*-methoxylobarate (7.42 μM), usimine A (15.0 μM), usnic acid (16.4 μM), usimine C (23.2 μM), usimine B (27.7 μM), lecanoric acid (31.0 μM), atranorin (63.5 μM); methyl orsellinate, methyl hematommate, and 2,6-dihydroxy-4-methoxy-3-methylacetophenone (> 200 μM).
Phospholipase A_2 [28]	Inhibition (IC_{50}) by orcinol (0.22 mM), methyl orsellinate (0.26 mM).

NMR AND IR SPECTRAL DATA

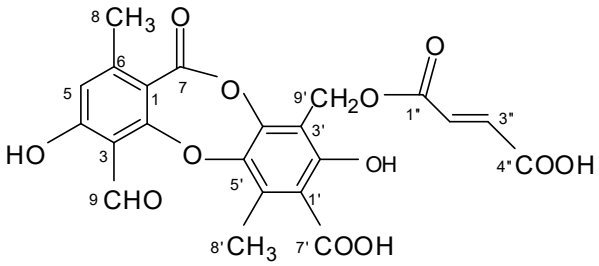
^{1}H- and ^{13}C-NMR SPECTRA



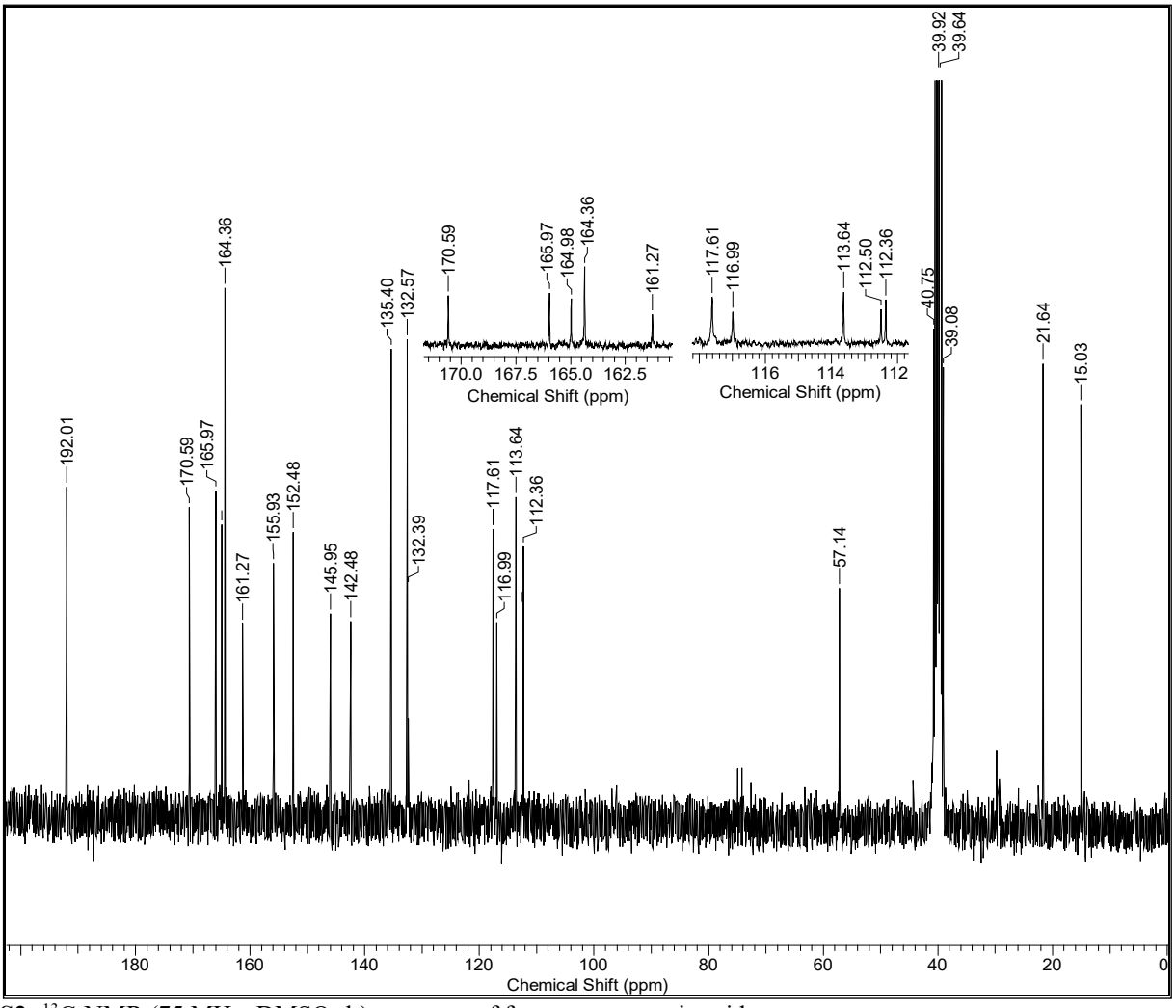
Fumarprotocetraric acid: δ (300 MHz, DMSO-d$_6$) 2.42 (3 H, s, H-8'), 2.44 (3 H, s, H-8), 5.29 (2H, s, CH$_2$-9'), 6.64 (2 H, s, H-2'' and H-3''), 6.83 (1 H, s, H-5), 10.56 (1 H, s, H-9), 11.98 (1 H, s, -OH).



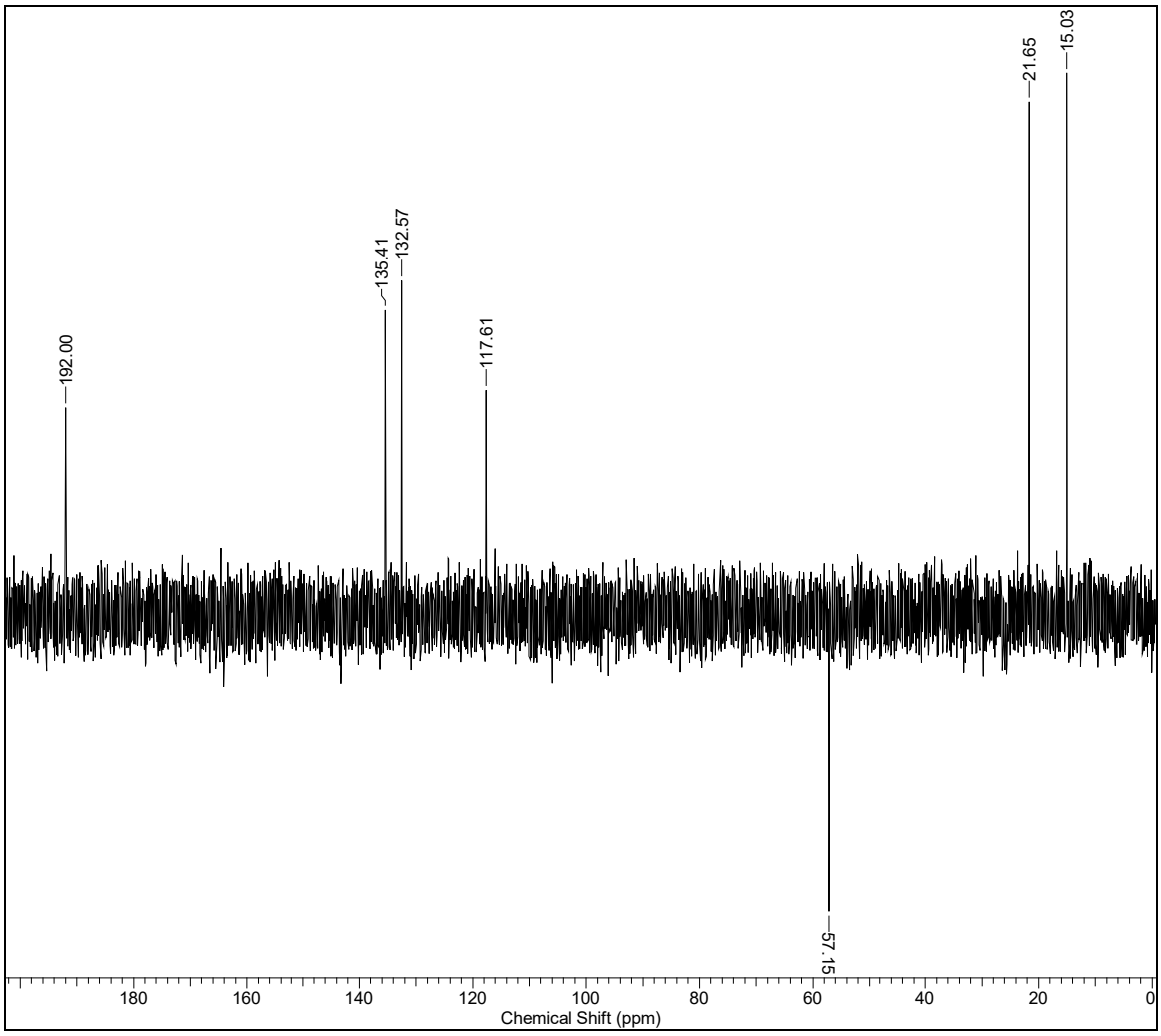
S1: ^{1}H-NMR (300 MHz, DMSO-d$_6$) spectrum of fumarprotocetraric acid.



Fumarprotocetraric acid: δ (75 MHz, DMSO-d_6) 112.5 (C-1), 166.0 (C-2), 112.4 (C-3), 165.0 (C-4), 117.6 (C-5), 152.5 (C-6), 161.3 (C-7), 21.6 (C-8), 192.0 (C-9), 117.0 (C-1'), 155.9 (C-2'), 113.6 (C-3'), 146.0 (C-4'), 142.5 (C-5'), 132.4 (C-6'), 170.6 (C-7'), 15.0 (C-8'), 57.1 (C-9'), 164.4 (C-1'' and C-4''), 135.4 (C-2''), 132.6 (C-3'').



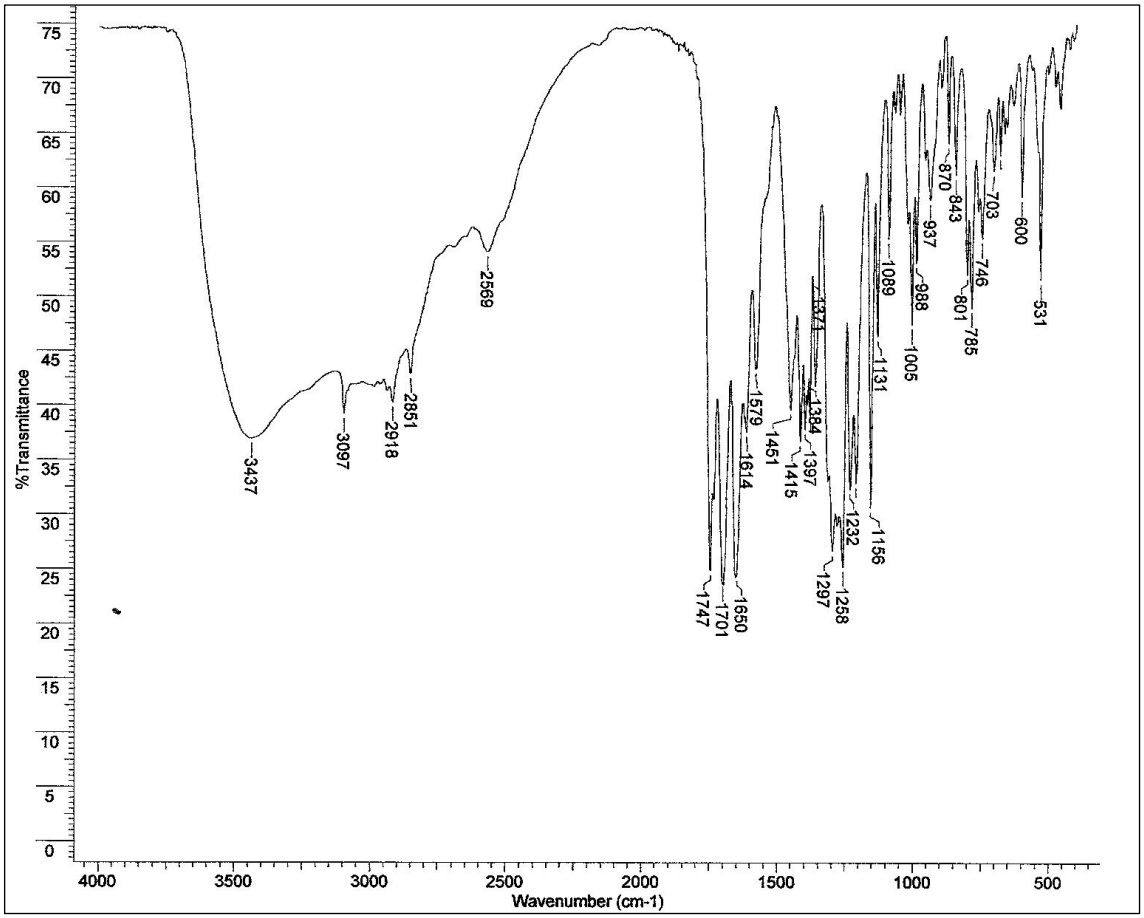
S2: ^{13}C-NMR (75 MHz, DMSO-d_6) spectrum of fumarprotocetraric acid.



S3: ^{13}C-NMR (DEPT-135) (75 MHz, DMSO-d_6) spectrum of fumarprotocetraric acid.

IR SPECTRAL DATA

Fumarprotocetraric acid (KBr): 3437, 2918, 2851, 1747, 1701, 1650, 1614, 1379, 1297, 1258, 1232, 1200 cm^{-1}.



S4: IR spectrum of fumarprotocetraric acid.