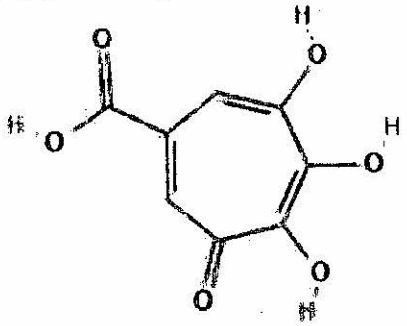
成分Xの構造同定

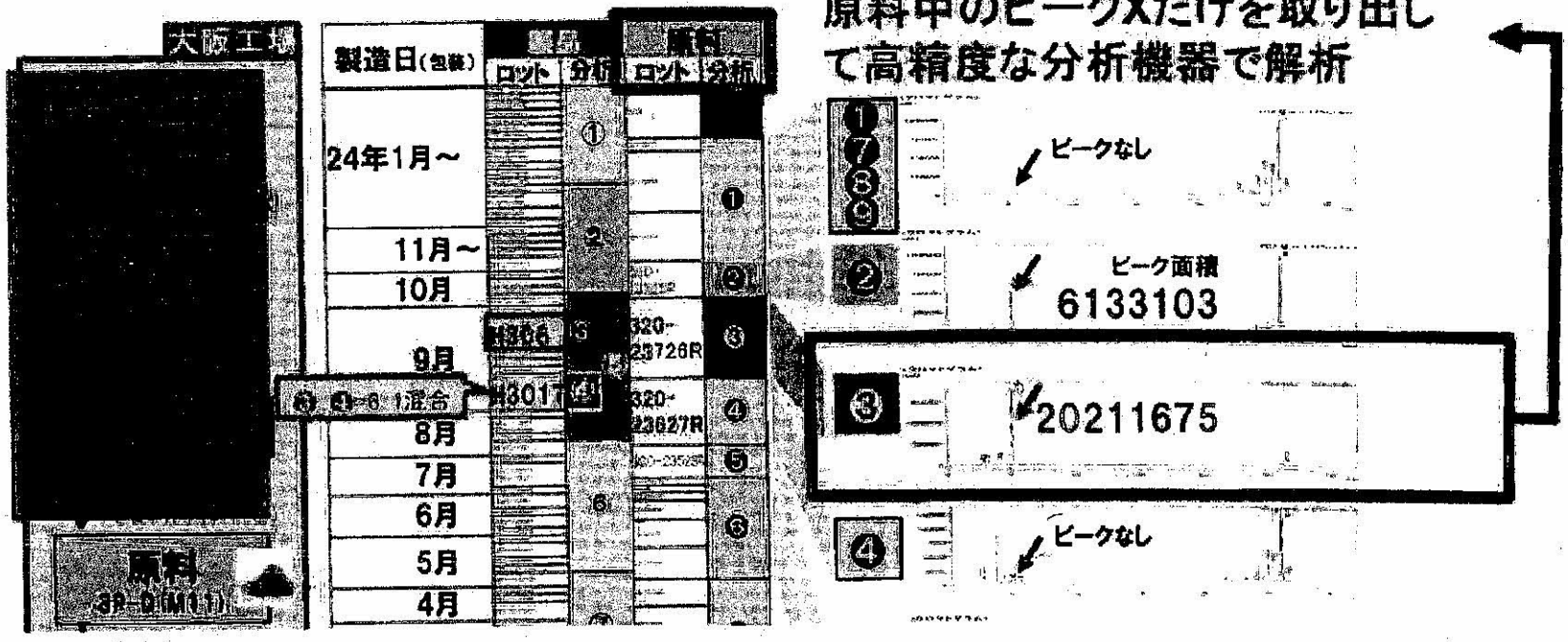
成分(=ピーク)X=Puberulic acidとして同定

ペニシリウム属(青カビ)から単離された化合物として報告あり
調査した限り、紅麹から精製した報告はなし



化合物名：Puberulic acid
分子式：$C_8H_6O_6$
分子量：198.13g/mol
https://pubchem.ncbi.nlm.nih.gov/compound/592860

最もピークXの面積が大きい、製品「H306」の紅麹原料「320-23726R」からピークXを分取



NMRによる構造同定

成分Xの水素（H）と炭素（C）の構造中の位置関係・存在数のシグナルを解析。
シグナルが合致する文献情報から、Puberulic acidと特定した。

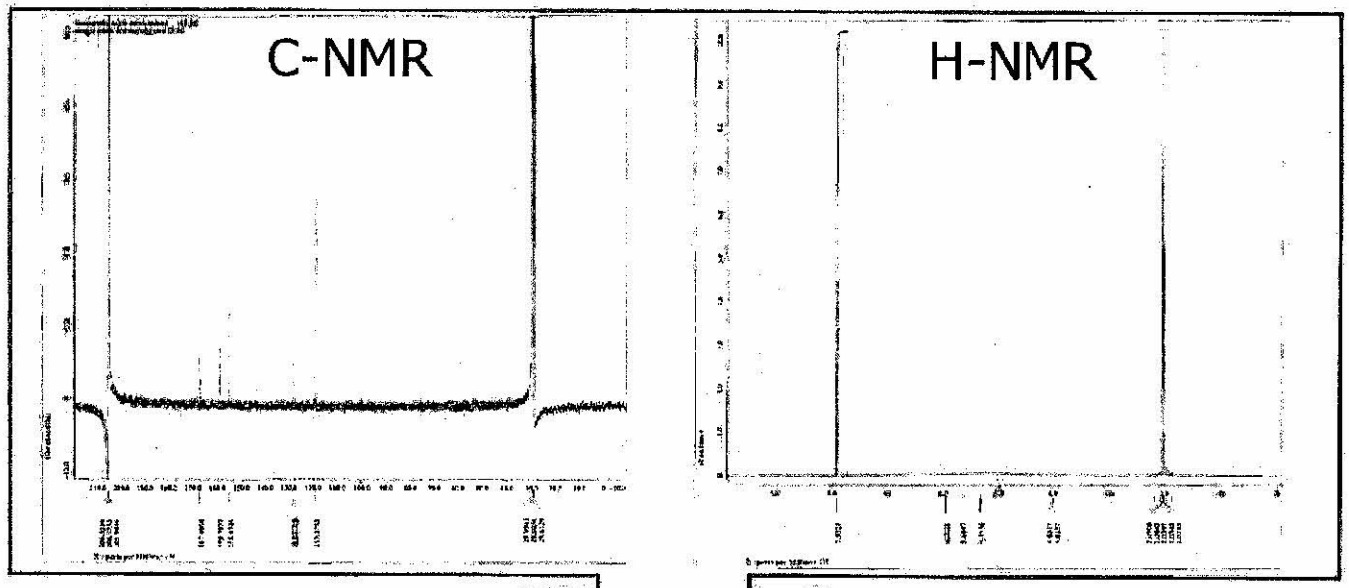
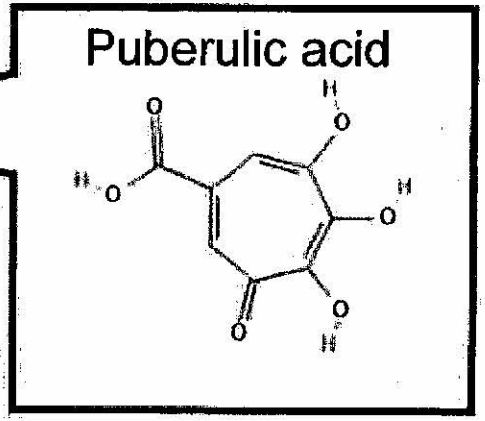


Table 2 ^{1}H and ^{13}C NMR spectral data of viticolins A–C (3–5), puberulic acid (1) and gliotatic acid (2)

	Viticolin A (3)[a]		Viticolin B (4)[a]		Viticolin C (5)[a]		Puberulic acid (1)[b]		[c]	
Position	^{13}C	^{1}H (J in Hz)	^{13}C	^{1}H (J in Hz)	^{13}C	^{1}H (J in Hz)	^{13}C	^{1}H (J in Hz)	^{13}C	^{1}H (J in Hz)
1	170.5	—	172.3	—	171.2	—	159.4	—	176.6	—
2	163.8	—	162.4	—	163.3	—	155.4	—	165.9[d]	—
2-OCH_3	—	—	56.9	3.97 (3H, s)	—	—	—	—	—	—
3	111.0	7.72 (1H, s)	109.8	7.55 (1H, s)	110.1	6.47 (1H, s)	119.3	7.96 (1H, s)	113.4	7.62 (1H, s)
4	133.0	—	130.2	—	158.2	—	128.4	—	139.1	—
5	122.5	7.83 (1H, s)	126.3	7.85 (1H, s)	110.2	—	119.3	7.96 (1H, s)	124.2	7.62 (1H, s)
6	161.0	—	158.0	—	169.1	—	155.4	—	169.3[d]	—
6-OCH_3	—	—	—	—	57.1	3.75 (3H, s)	—	—	—	—
7	152.0	—	151.0	—	114.2	6.59 (1H, s)	159.4	—	117.4	6.95 (1H, s)
7-OCH_3	58.8	3.94 (3H, s)	60.1	3.87 (3H, s)	—	—	—	—	—	—
8	167.0	—	168.8	—	70.3	5.10 (2H, s)	167.4	—	168.5	—
9	—	—	—	—	170.1	—	—	—	—	—

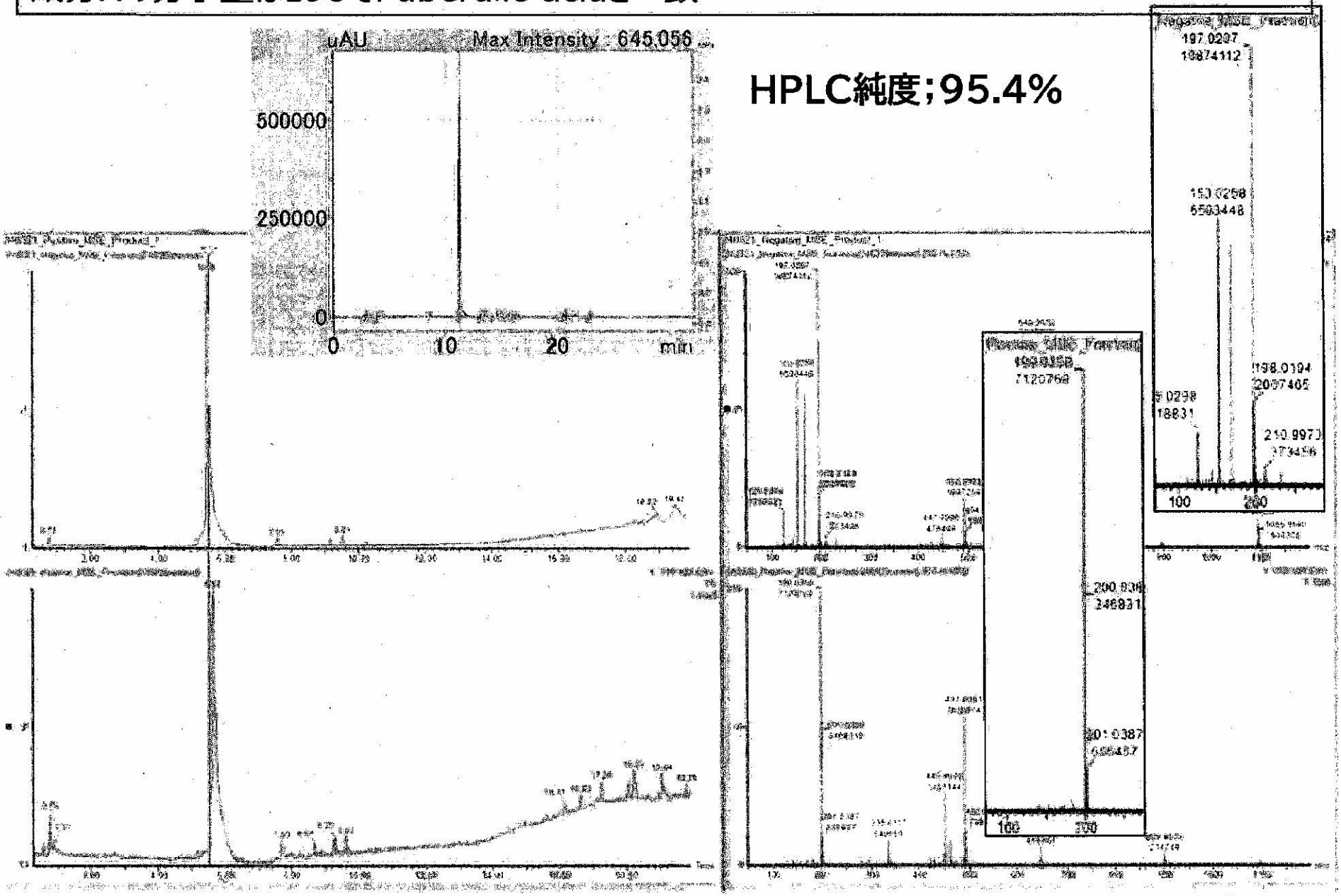
[a]Measured in CD_3OD.
[b]Measured in DMSO-d_6 + 5% CD_3OH.
[c]Measured in acetone-d_6.
[d]Exchangeable.



The Journal of Antibiotics (2011) 64, 183–188

超高精度質量分析

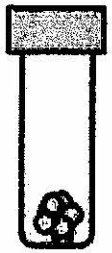
成分Xの分子量は198でPuberulic acidと一致



成分Xの含有量

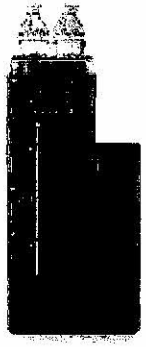
[検量線の作成]

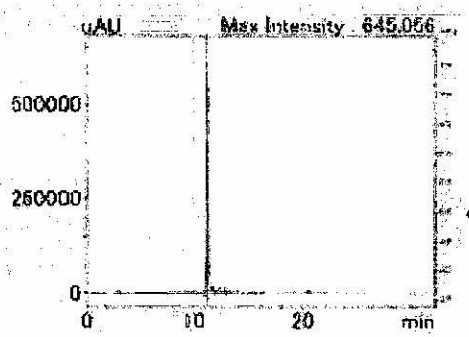
濃度既知の溶液調製



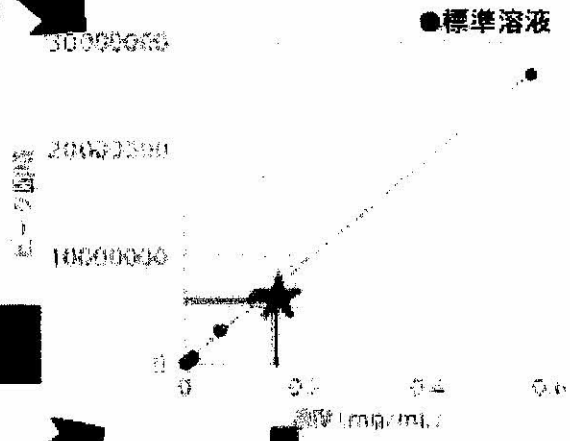
単一に精製
した成分X

機器分析



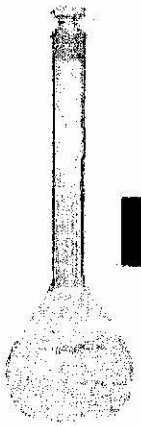


検量線と含量計算

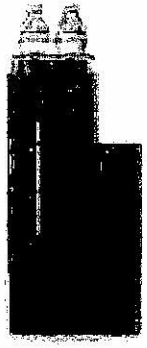


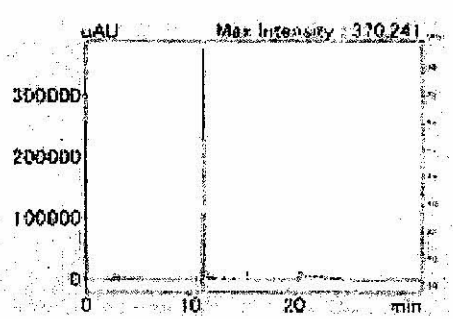
[試料溶液の測定]

成分の抽出



機器分析

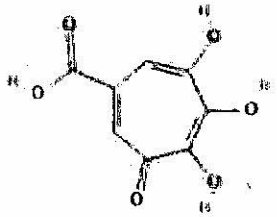




調製方法から
含有量計算

成分Xの公知情報（簡易調査）

Puberulic acid



①抗生剤としての特徴がある
抗細菌活性があることが古くから知られる抗生剤
※近年、高い抗マラリア原虫活性が報告されている

②アオカビが産生する
複数のPenicillium属菌（=アオカビ）が産生する報告あり

③多くの抗生剤は腎障害を引き起こすことが知られている
Puberulic acidと類似の化合物(トロポロンナトリウム)を投与したマウスにおいても腎組織悪化（組織学的変化）が見られる報告あり

SCIENTIFIC REPORTS

Antimalarial troponoids, puberulic acid and viticolins; divergent synthesis and structure-activity relationship studies

Goh Sennari1, Ryo Saito1, Tomoyasu Hirose1,2, Masato Iwatsuki1,2, Aki Ishiyama2, Rei Hokari2, Kazuhiko Otoguro2, Satoshi Ōmura2 & Toshiaki Sunazuka1,2

Puberulic acid (1)[7], stipitatic acid (2)[8] and viticolins A and B (3, 4) as novel natural products have been isolated from a culture broth of *Penicillium viticola*[9] FKI-4410 through our screening system and found to have promising antimalarial activity (Fig. 1)[10,11]. In these highly-oxygenated 7-membered aromatic compounds, 1 shows the most potent antimalarial activity *in vitro* against the *Plasmodium falciparum* K1 (chloroquine-resistant) parasite strain (IC_{50} = 0.050 μM), as well as *in vivo* efficacy with 69% inhibition for a dose of 2 mg/kg × 4 through subcutaneous (s.c.) administration in 4-day suppressive test using a *P. berghei*-infected mouse model[12]. However, 1 exhibits toxicity *in vivo*, four out of five mice dying by day 3, after a s.c. dose of 5 mg/kg × 2 (day 0 and 1). While structually simple compounds such as tropone (5), tropolone (6) and hinokitiol (8), and natural 2 and 3 showed weaker activity than that of 1, 7-hydroxytropolone (7)[13] was much more potent, exhibiting a >18-fold stronger IC_{50} value of 6.44 μM than that of 5. This observation suggested that the presence of more than three contigu-