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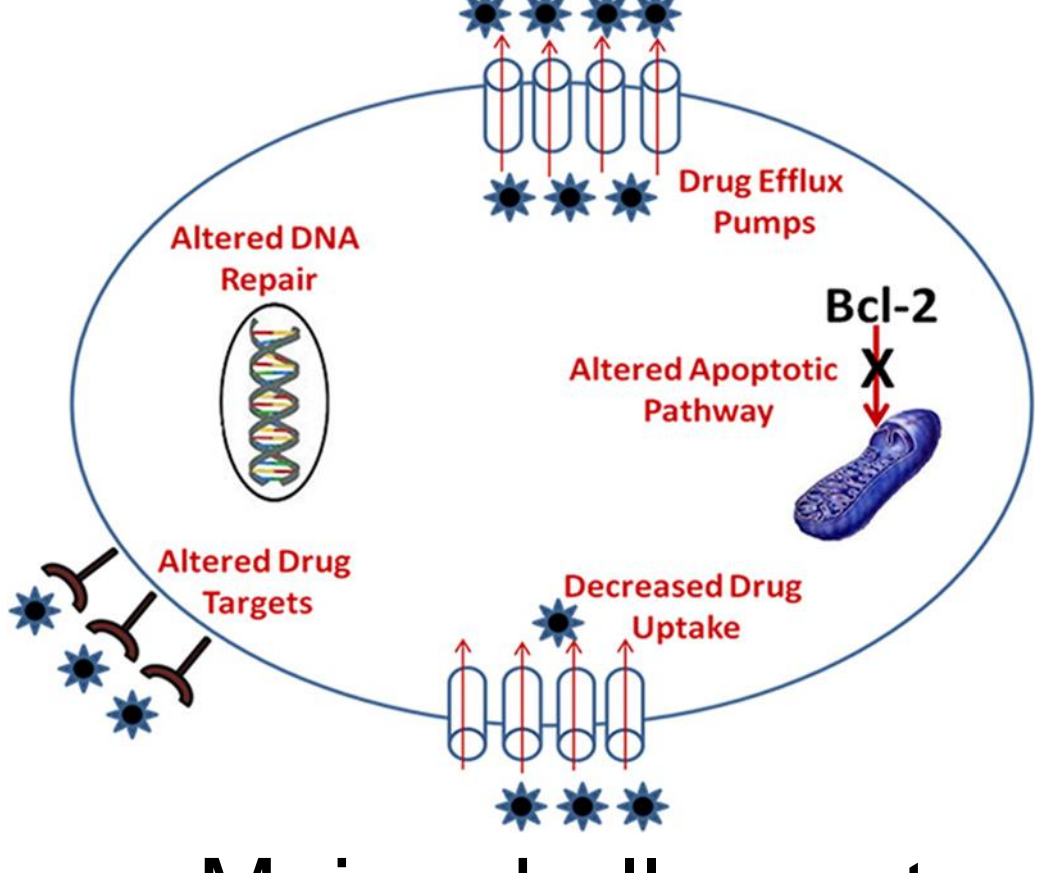
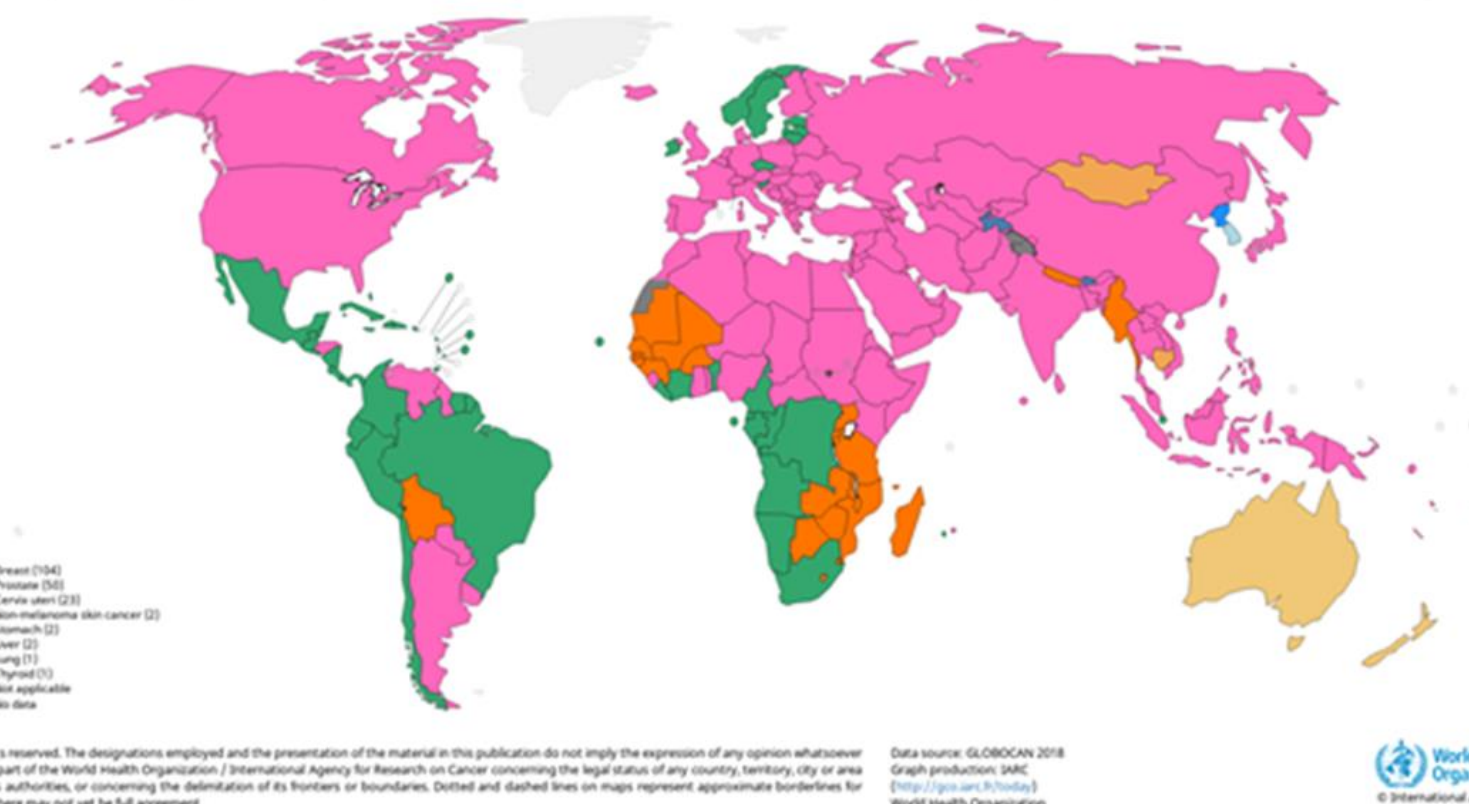
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## Introduction

Top cancer per country, estimated age-standardized incidence rates (World) in 2018, both sexes, all ages



• Major challenge to cancer therapy

Despite the great development in Human medicine, cancer is still a serious threat to public health and consequently, research on new anticancer agents should be continued. Medicinal plants (e.g., *Plectranthus* species) continue to be a substantial resource. diterpenoids, which are reported to be responsible for various pharmacological activities such as cytotoxic activity [1,2,3]. *P. mutabilis* Codd. is a perennial succulent herb containing Nepetoidins A and Nepetoidins B in its essential oils with limited information available in the literature [3].

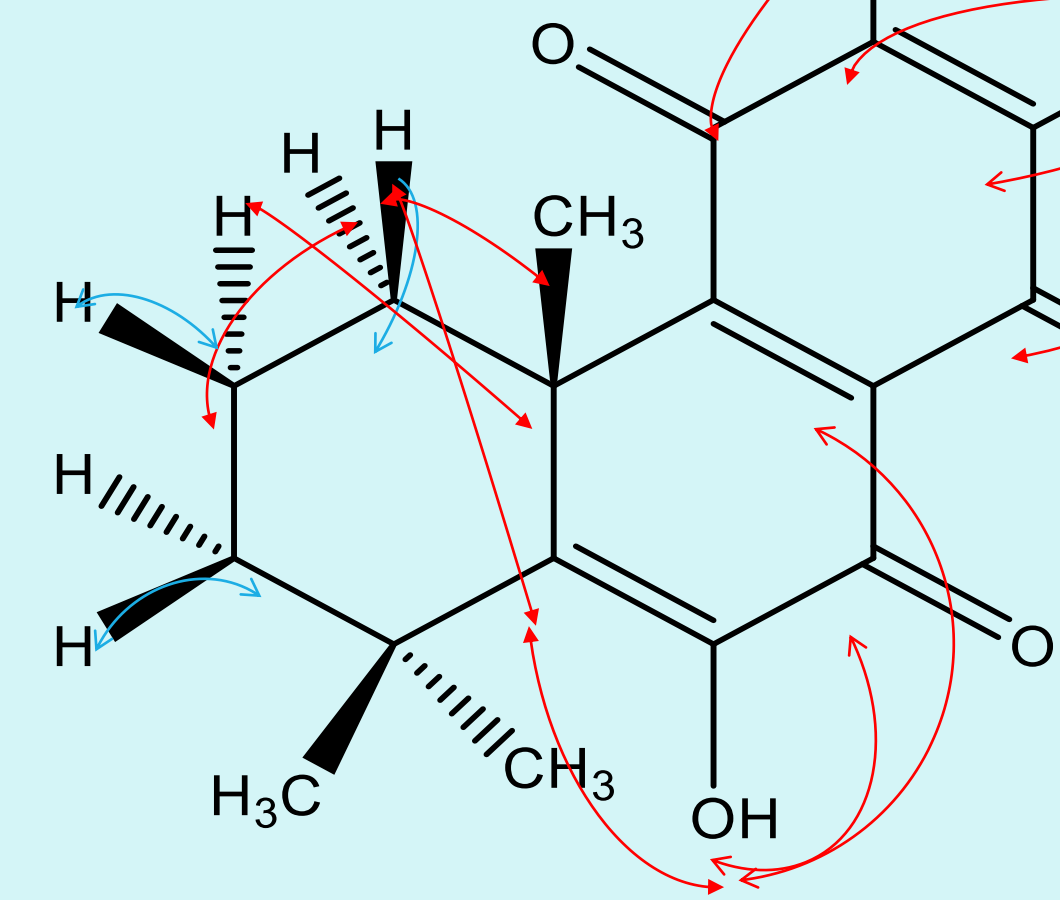
• Cancer is still a serious threat to public health

## Methods and Results

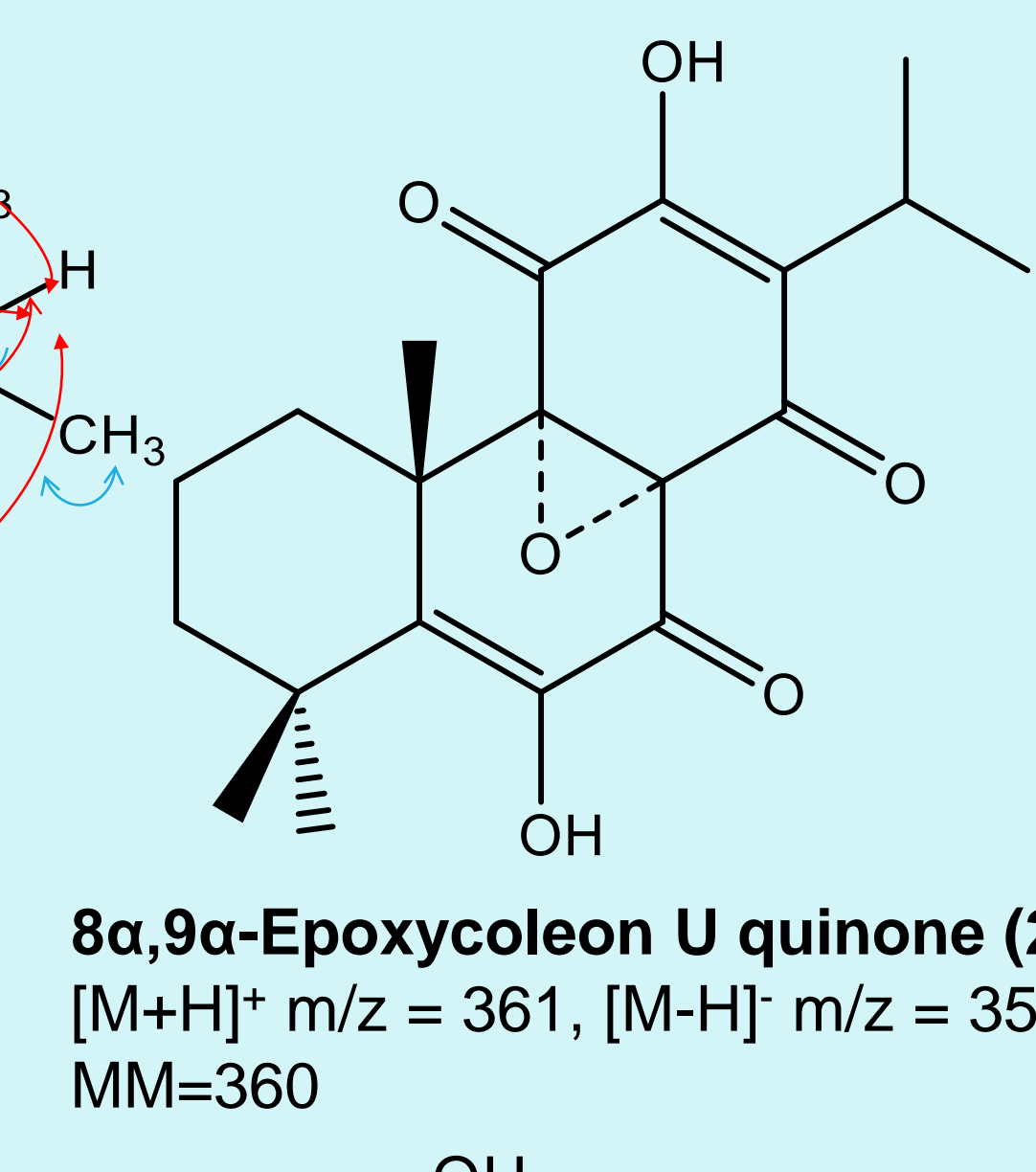
### Isolated compounds

HMBC – red arrows

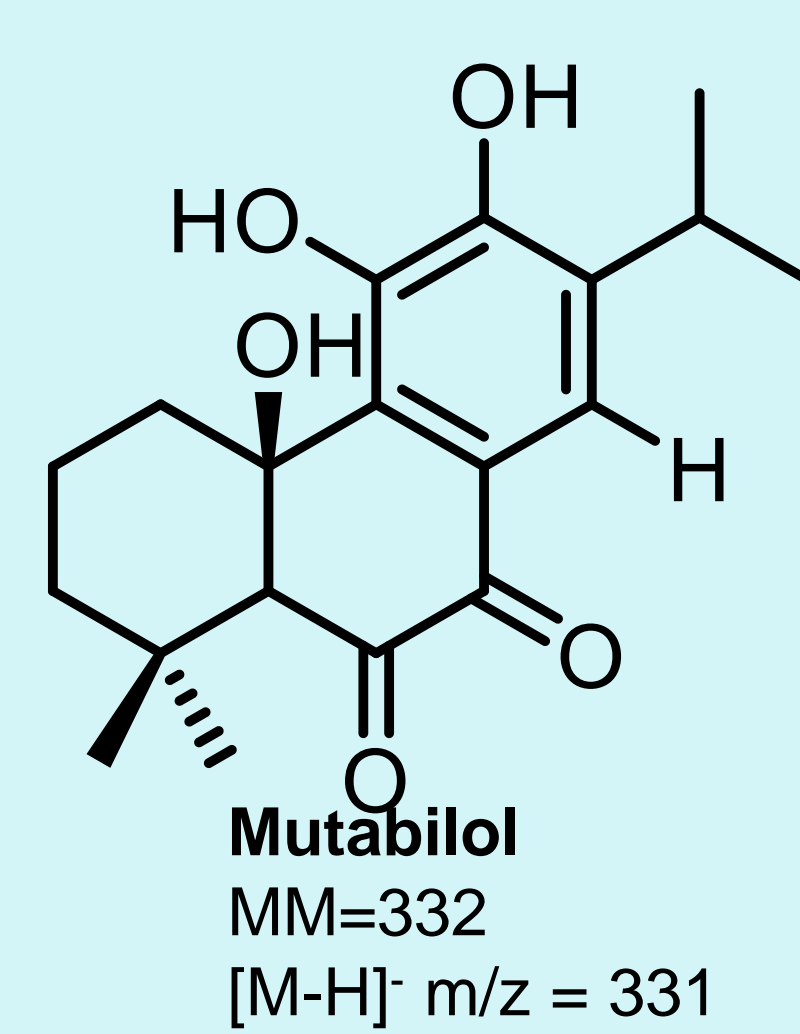
HMQC – blue arrows



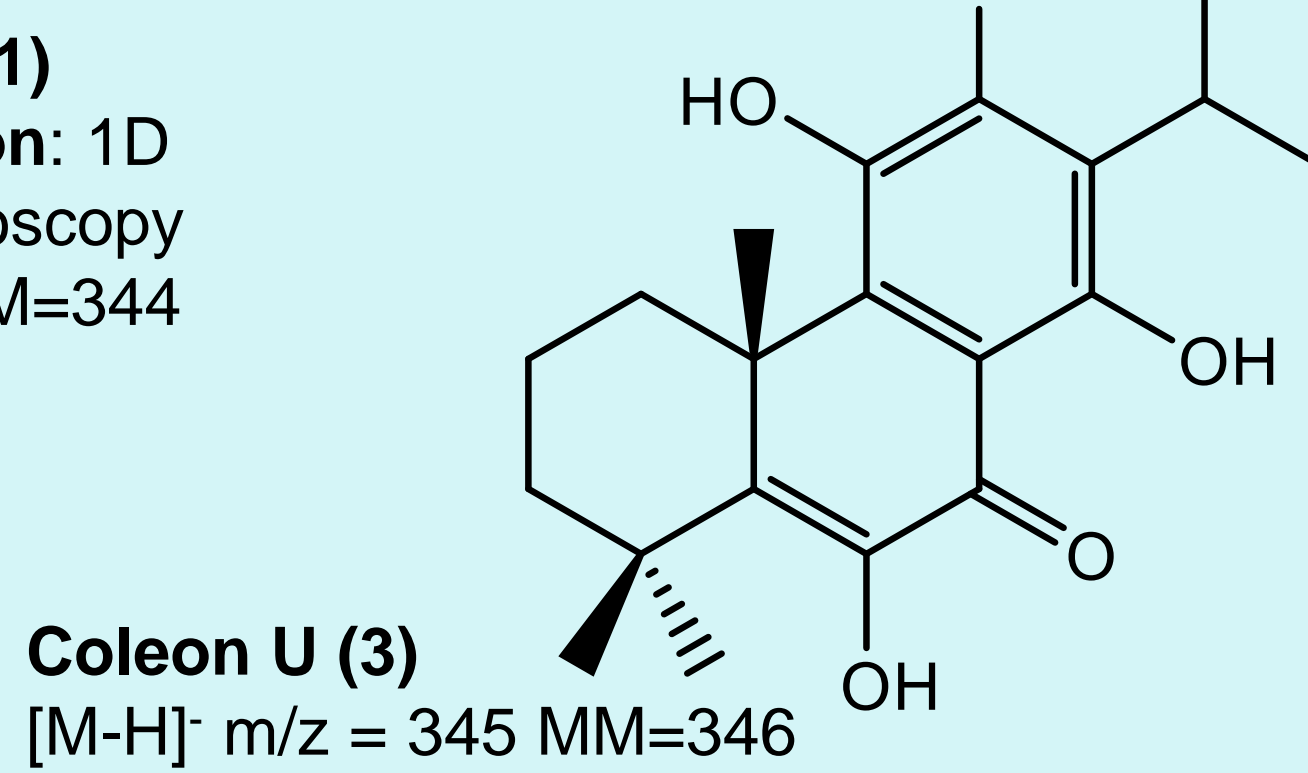
**Coleon U Quinone (1)**  
structure elucidation: 1D and 2D NMR spectroscopy  
[M+H]<sup>+</sup> m/z = 345 MM=344



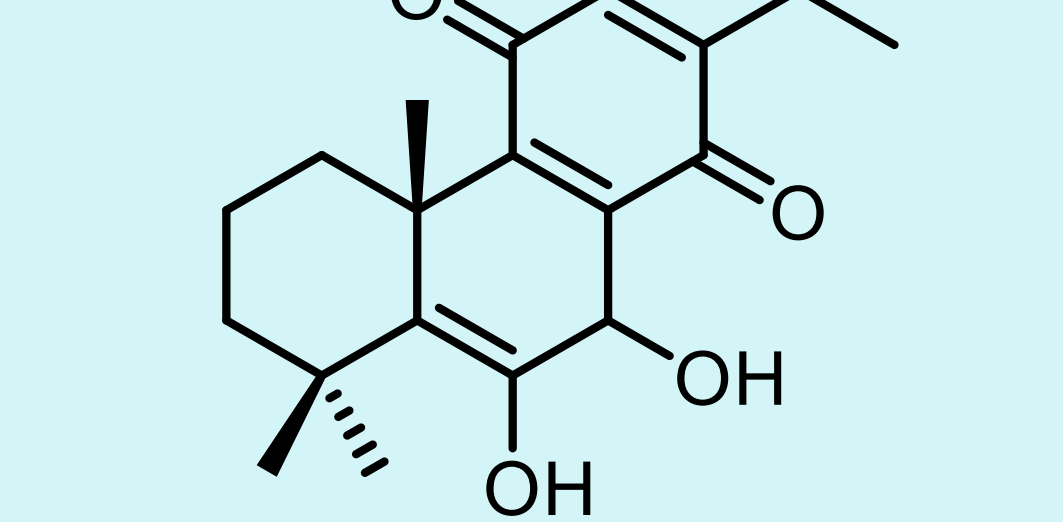
**8α,9α-Epoxycoleon U quinone (2)**  
[M+H]<sup>+</sup> m/z = 361, [M-H]<sup>-</sup> m/z = 359  
MM=360



**Mutabilol**  
MM=332  
[M-H]<sup>-</sup> m/z = 331



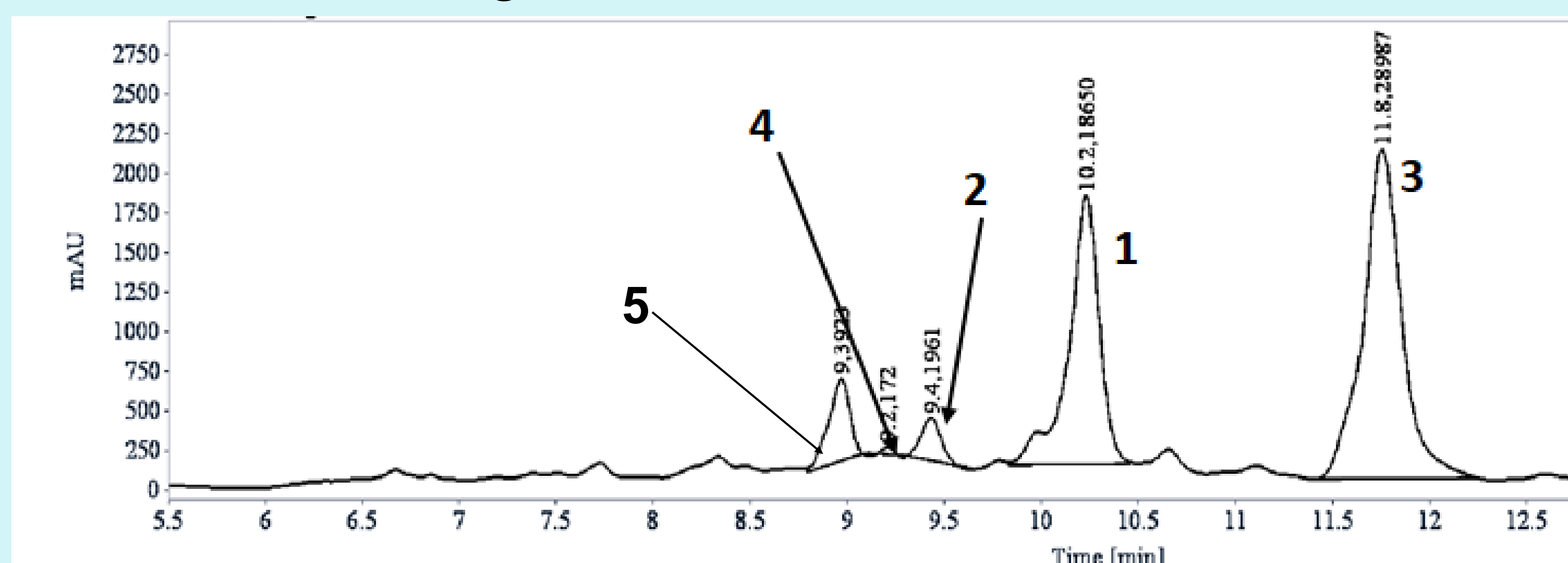
**Coleon U (3)**  
[M-H]<sup>-</sup> m/z = 345 MM=346



**12-O-Acetylcoleon U quinone (5)**  
LCMS results. Tentatively identified

Structural elucidation: 1D-and 2D-NMR and LC/MS

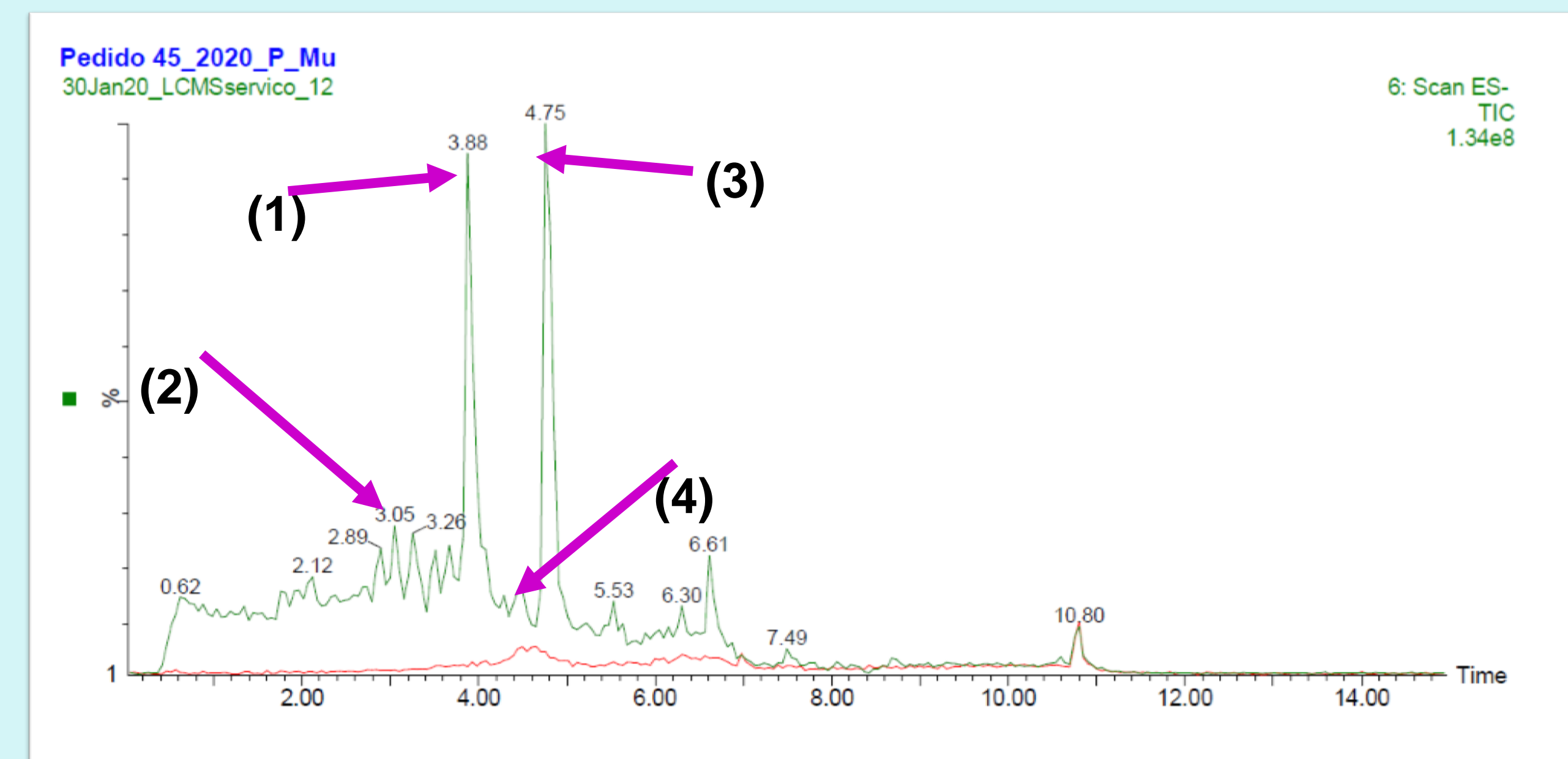
### HPLC–DAD Profiling of *P. mutabilis* acetonic extract



**UV detection:**

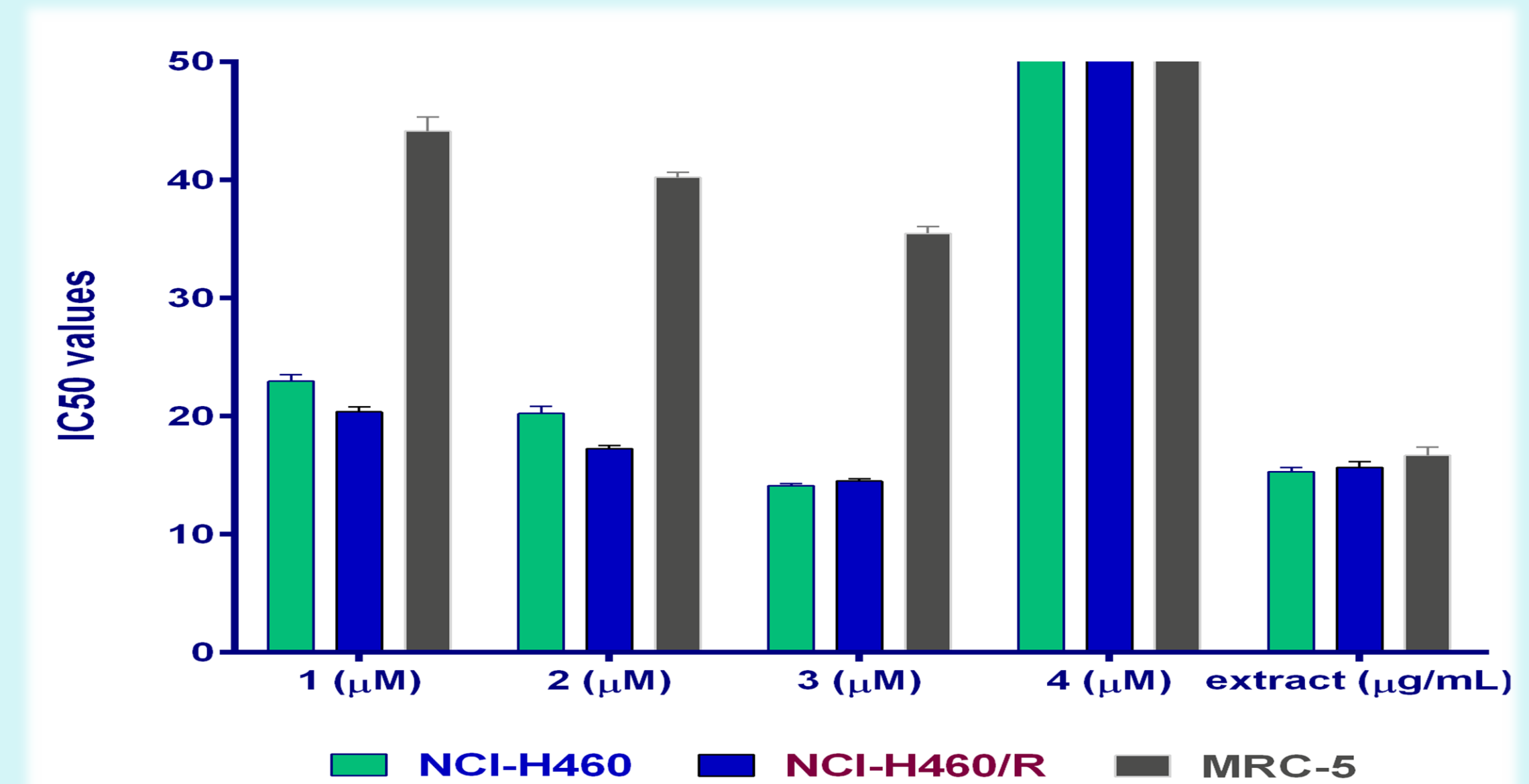
- 270 for 1 and 2;
- 254 for 3 and 4

### LC/MS analysis of 4 compounds from *P. mutabilis*



Comparison of chromatographic profiles of 4 isolated compounds with *P. mutabilis* extract

Inhibition of cell viability assayed by MTT in non-small cell lung cancer cells (NCI-H460 and NCI-H460/R) and embryonal pulmonary fibroblasts (MRC-5).



### Rhodamine 123 accumulation assay after 30 min of exposure

Compounds/(Cell Lines)	MFI <sup>a</sup>	FAR±S.E. <sup>b</sup>	SI±S.E. <sup>c</sup>
NCI-H460 <sup>d</sup>	2479.3	3.06±0.61	
NCI-H460/R	811.1		32.71±1.65
<b>TARIQUI</b>			
<b>DAR</b>	50 nM	3004.0	<b>3.70±0.54<sup>e</sup></b>
<b>Extract</b>	5 µg/mL	339.5	0.42±0.20 <sup>f</sup>
	10 µg/mL	307.7	0.38±0.20
<b>1</b>	5 µM	277.3	0.34±0.20
	10 µM	242.0	0.30±0.20
<b>2</b>	5 µM	289.7	0.36±0.20
	10 µM	276.6	0.34±0.21
<b>3</b>	5 µM	173.5	0.21±0.24
	10 µM	109.7	0.14±0.29
<b>4</b>	5 µM	265.9	0.33±0.21
	10 µM	254.5	0.31±0.22

Compounds	conc. µg/mg	LOD µg/mg	LOQ µg/mg
Coleon U (3)	96±0.048	0.78	2.35
Coleon U quinone (1)	35±0.005	0.102	0.310
Mutabilol (4)	51±0.008	1.120	3.39
8α,9α-Epoxycoleon U quinone (2)	36±0.018	0.828	2.510

Results are expressed as average ± standard deviation (SD) of three determinations. LOD (limit of detection) and LOQ (limit of quantification).

- **Tariquidar** increases the accumulation of Rhodamine 123 and thus inhibits P-gp activity
- All tested compounds and extract **decreased** the Rhodamine 123 accumulation
- Compounds and extract **stimulate** P-gp activity.
- More studies are ongoing to understand the mechanism of action of these compounds

## References

[1] Ramzi A, Jamal M, Omar M, Ashok K, Mohamed F, Adnan J, Mine K., BMC Complement Altern Med. 2018; 18: 237  
 [2] Diogo M, Marisa N, Lucília S, Rute P, Célia F, Ana D, Catarina P, Tijana S, Jelena D, Milica P, Patrícia R., ACS Omega 2019, 4, 5, 8094–8103  
 [3] Ntungwe, E.; Domínguez-Martín, E.M.; Teodósio, C.; Teixidó-Trujillo, S.; Armas Capote, N.; Saraiva, L.; Díaz-Lanza, A.M.; Duarte, N.; Rijo, P. *Pharmaceuticals* 2021, 14, 402.  
 [4] Gray R, Eckert MR, Lever A, Veitch NC, Kite GC, and Paton AJ., *Phytochemistry*. 2003; 64:519–528

## Conclusio

- ✓ ***P. mutabilis*: a source of abietane diterpenoid**–Coleon U quinone, 8α,9α-Epoxycoleon U quinone, Coleon U, mutabilol
- ✓ All the compounds are present in the extract Coleon U is the major compounds in *P. mutabilis* extract
- ✓ Compounds **1, 2** and **3** are selective towards cancer cells due to lower IC<sub>50</sub> in cancer cells (NCI-H460 and NCI-H460/R) than in normal bronchial fibroblasts (MRC-5).
- ✓ Compound **4** is not cytotoxic in a given range of concentrations (2 to 50 microM).
- ✓ All compounds are not substrates for P-gp