Supplementary Information

Method of Roxy determination

Using TLC F_{254} silica gel plates as a stationary phase and methanol-acetone-ammonia 25% (1:14:0.1, v/v/v) as the mobile phase, selected based on testing twenty different mobile phases, compact, well-developed and resolved peaks of Roxy and its degradation products formed during acidic hydrolysis were obtained, enabling their determination. Characteristic absorption spectra registered directly from chromatograms after visualization of spots with sulfuric acid in ethanol (data not shown) showed a maximum at 483 nm, which was chosen as the analytical wavelength for Roxy and its degradation products. The results of the method validation are presented in **Table S1.** Validation results have shown high sensitivity, accuracy, precision and wide linearity range of the method. The correlation coefficient obtained for linear model was greater than 0.99. The distribution of residuals could be well approximated with a normal distribution as shown by the p-value (p>0.05) of the Shapiro-Wilk normality test. Based on regression analysis it was assumed that the calibration data fitted well to a linear model. The usefulness of the method for the environmental and pharmaceutical analyses was checked based on quantitative analysis of the available pharmaceutical preparations.

Method validation

The optimized method was validated for the determination of Roxy in the presence of its degradation products according to the ICH guidelines [ICH Q2 (R1), Validation of Analytical Procedure: Text and Methodology, 2005].

Specificity

The specificity of the method was ascertained by the analysis of the solution of Roxy obtained after hydrolysis in acidic solutions and comparison with analysed standard solution. The spots were identified by R_F values for Roxy and its degradation products.

Linearity

To check linearity of the method 5, 10, 15, 20, 25 μL of Roxy standard solution were applied to the 12×15 cm plate. Linearity was determined based on the relationship between the peak areas and Roxy mass (μg/spot). The regression plot, regression equation, coefficient of determination r^2 and the distribution of residuals by Shapiro-Wilk normality test were calculated by Statistica 10.0 and are indicative of linearity.

Precision

The intraday and interday precision of the method was derived from the degree of consistency of the recorded peak areas for Roxy standard solution. Five determinations were made by applying 1.5 μg/spot at 50% level, 3 μg/spot at 100% level, 4.5 μg/spot at 150% level to the plate followed by the analysis according to the method conditions. The interday precision was carried out after one week by a different analyst. The precision was estimated using peak areas and was evaluated as the standard deviation (SD) and relative standard deviation (RSD) values.

LOD and LOQ

To determine the limit of detection (LOD) and limit of quantitation (LOQ), concentrations of Roxy in the lower part of the linear range of calibration curve were used. Five, 7, 10, 15 and 20 μL of Roxy standard solution at a concentration of 0.0025% (w/v) were applied to the plate. Using standard error of the estimate and slope of a straight line coefficient, LOD and LOQ values were determined according to the following equations: $LOD = 3.3 \times S_e/a$, $LOQ = 10 \times S_e/a$; where S_e = standard error of the estimate and a = slope of a

straight line.

Recovery

Recovery studies were carried out by standard addition method. Roxy corresponding to 80, 100 and 120% of the label claim was added to pre-analyzed tablet sample solution, and each of the solutions was re-analyzed in triplicate.

Robustness

To examine robustness, the most significant chromatographic parameters were changed within the range of 1-5% compared to those of the optimal conditions, while keeping the other parameters unchanged. The following parameters were examined: proportions of methanol and acetone in the mobile phase, volume proportions in visualizing mixture, plate heating time and temperature. The influence of the stationary phase was also checked by application to HPTLC plates instead of TLC plates.

Table S1
**Summary of the validation results for the determination of Roxy**

Parameter	Result
R_F	0.42
Linearity	Linearity range [μg/spot]: 1.25 – 6.25 $P = a\,c + b$ a=2869.9; b=2216.9 S_a=128.45, S_b=532.53 r=0.9970; r^2=0.9940 Shapiro-Wilk normality test: W=0.90361 p=0.43016
LOD [ng/spot]	50
LOQ [ng/spot]	150
Accuracy [%] n=5	Level 80%: x_{mean}=98.27 SD= 0.84, RSD=0.85% Level 100%: x_{mean}=100.28 SD= 1.36, RSD=1.36% Level 120%: x_{mean}=98.95 SD= 1.20, RSD=1.21%
Intra-day precision	
50% level, n=5	x_{mean}=6543.42 SD= 170.44, RSD=2.60%
100% level, n=5	x_{mean}=10441.96 SD= 266.52, RSD=2.55%
150% level, n=5	x_{mean}=15053.56 SD= 181.35, RSD=1.20%
Inter-day precision	
n=5	x_{mean}=9818.76 SD= 108.89, RSD=1.11%

Note: P-peak area; c-concentration; r-correlation coefficient;
SD-standard deviation; RSD-relative standard deviation (%);
S_a-standard deviation of slope; S_b-standard deviation of intercept

Table S2
The results of Roxy determination in the pharmaceutical preparations with statistical analysis.

| Preparation	Declared content [mg/tablet]	Determined content range	Statistical analysis (n=6)
Rulid	150	149.04-154.95	x_m=152.58 SD=2.78 RSD=1.82%
Xitrocin	150	147.50-149.83	x_m=148.41 SD=1.23 RSD=0.83%
Rolicyn	150	145.07-148.56	x_m=146.99 SD=1.13 RSD=0.77%
Renicin	150	145.21-148.75	x_m=147.74 SD=1.29 RSD=0.87%

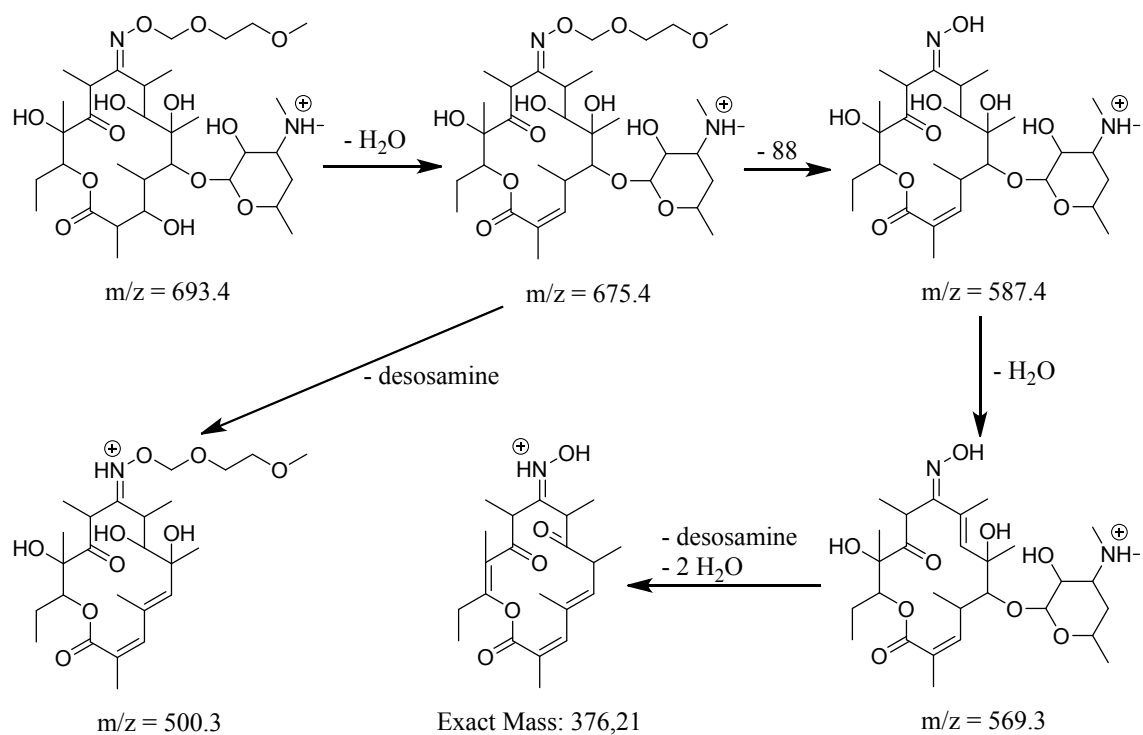Note: x_m-arithmetic mean, SD-standard deviation, RSD-relative standard deviation(%)
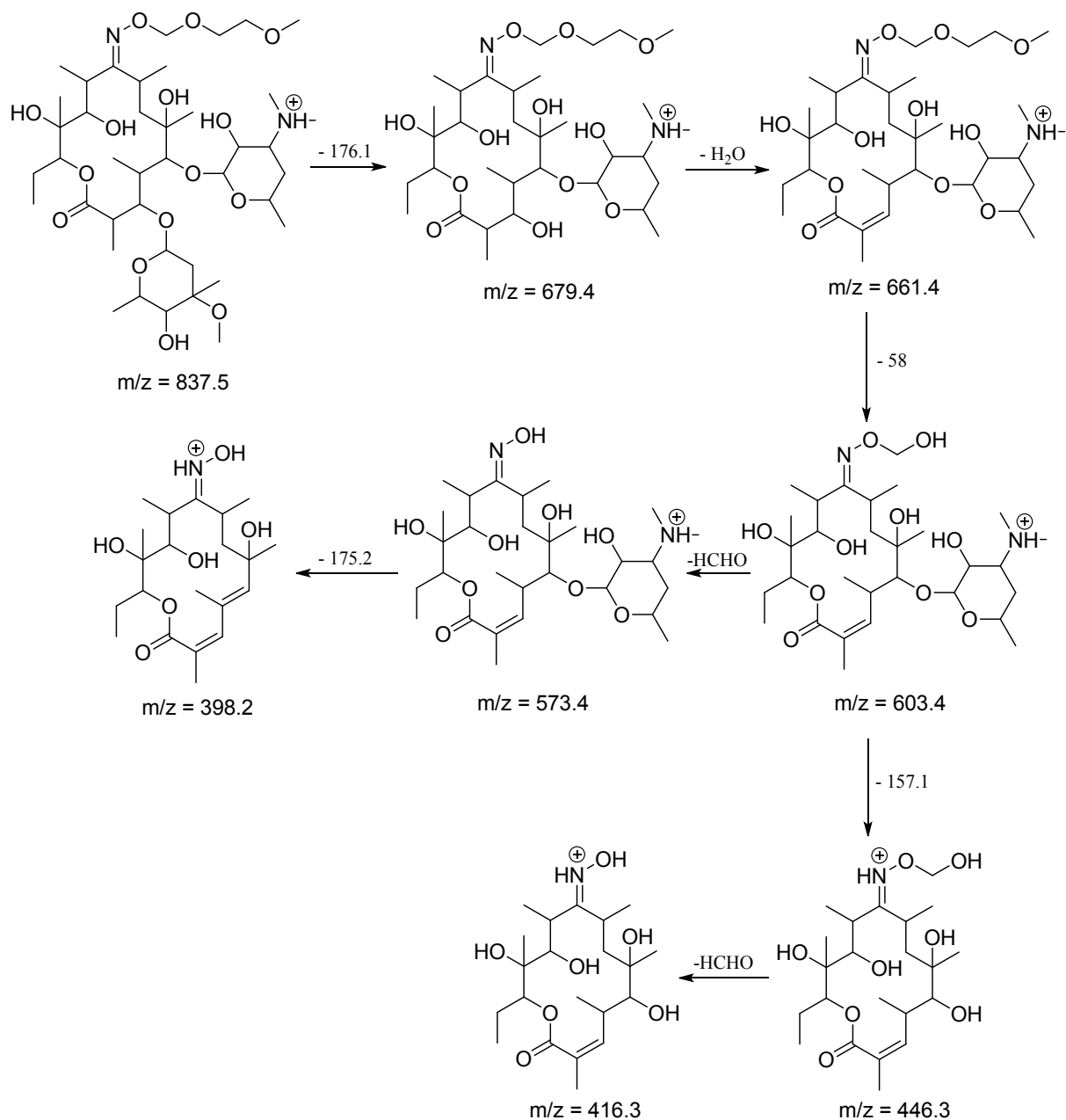
Scheme S1 Proposed fragmentation pattern of roxithromycine.
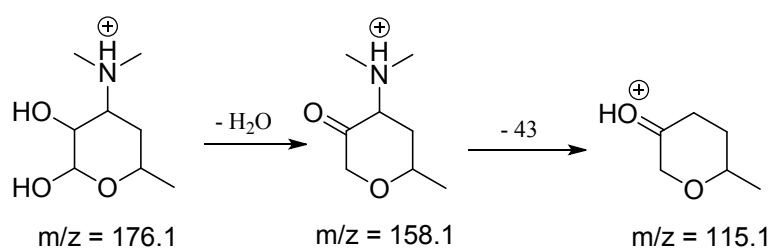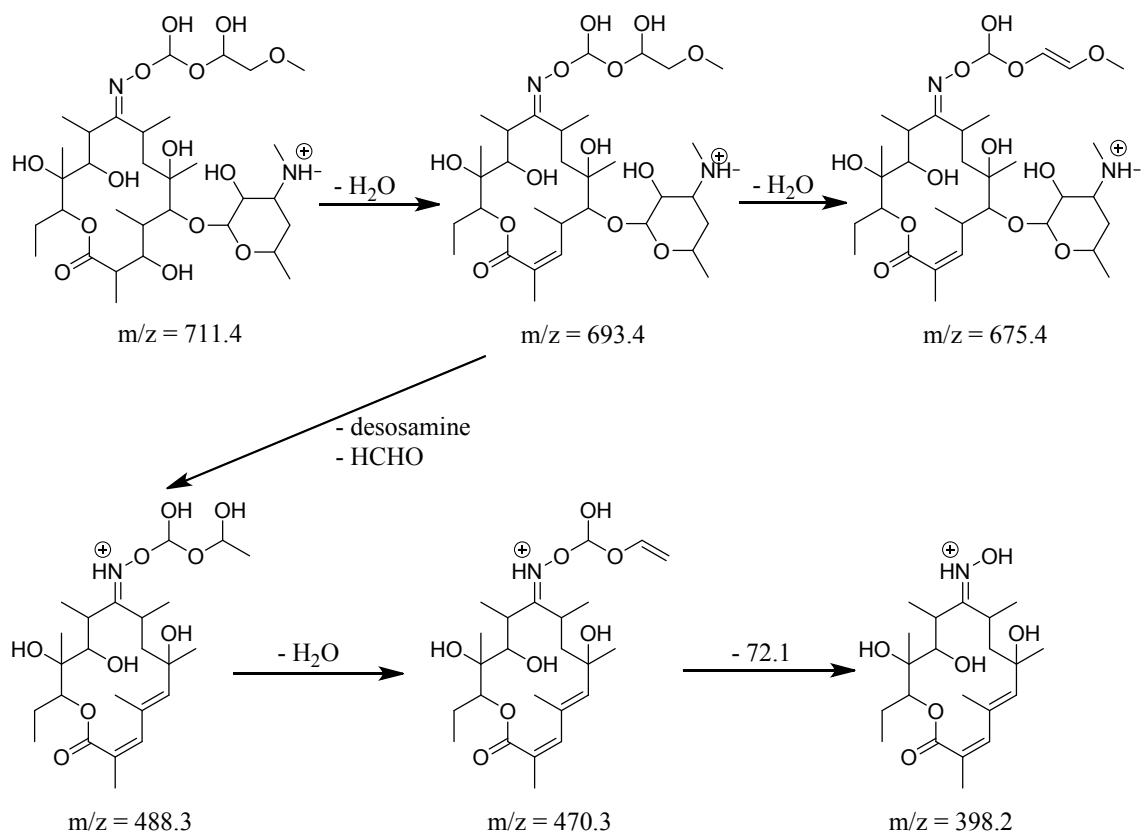

Scheme S2 Proposed fragmentation pattern of desosamine.
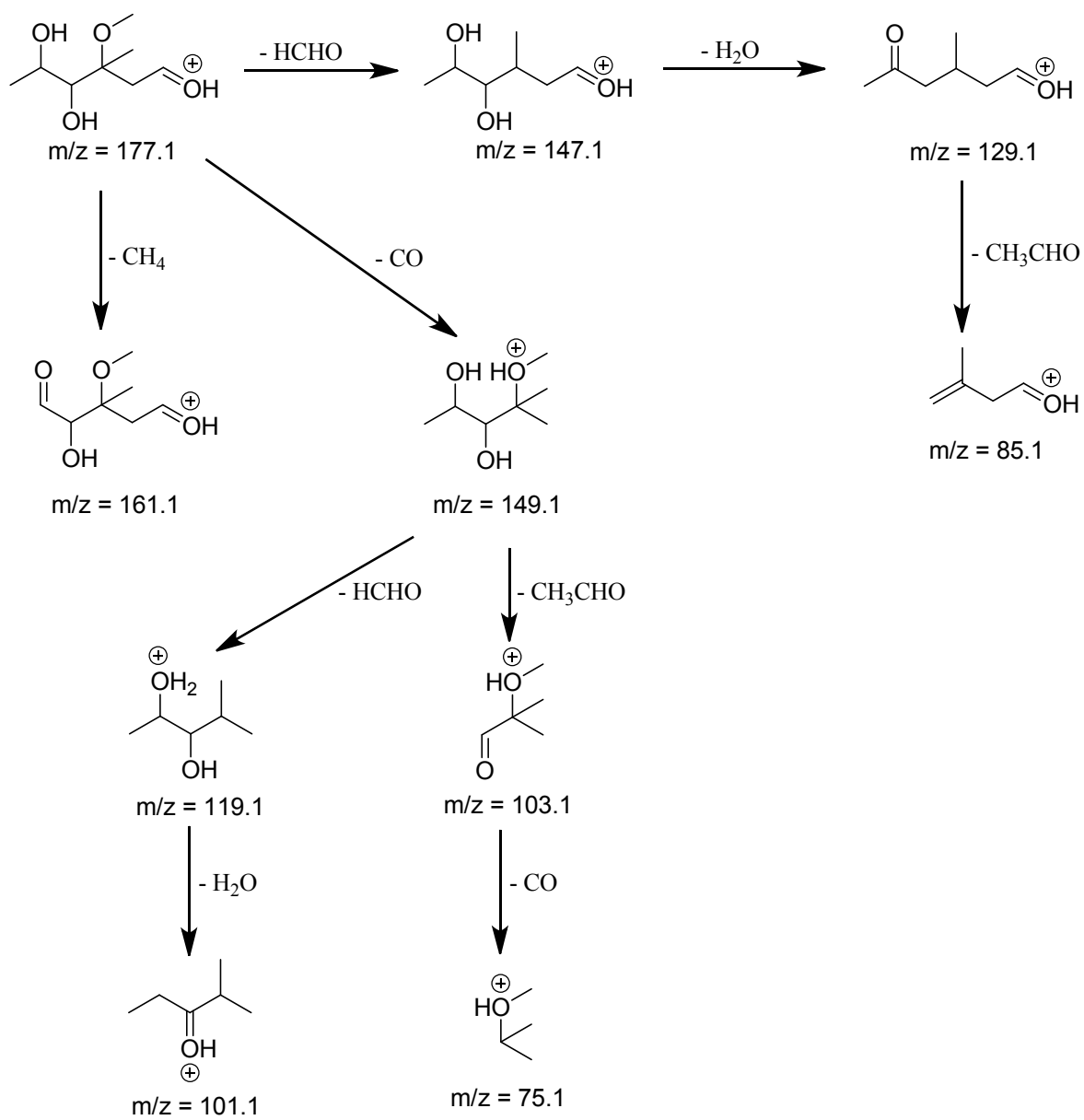
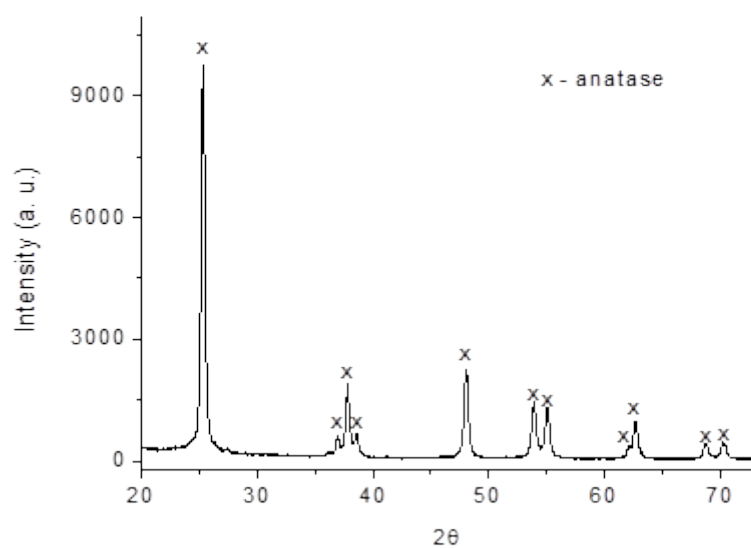**Scheme S3 Proposed fragmentation pattern of L-cladinose.**
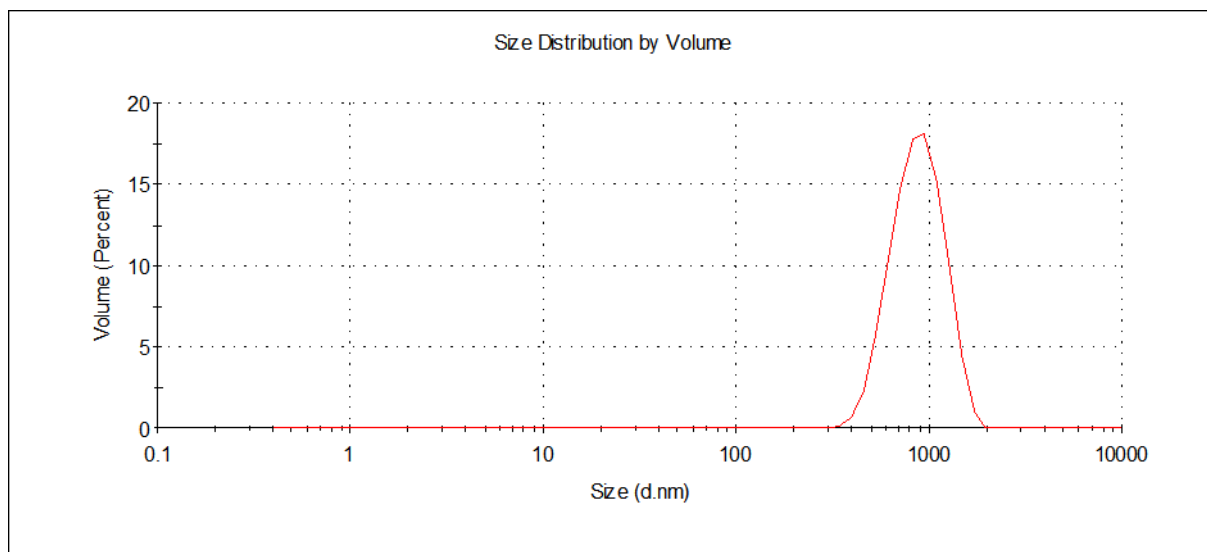
Scheme S4 Proposed fragmentation pattern of RP-UV-1.

m/z = 693.4   − H₂O   m/z = 675.4   − 88   m/z = 587.4

− desosamine

− H₂O

m/z = 500.3   Exact Mass: 376,21   m/z = 569.3

− desosamine
− 2 H₂O

Scheme S5 Proposed fragmentation pattern of RP-UV-5.

m/z = 711.4   − H₂O   m/z = 693.4   − H₂O   m/z = 675.4

− desosamine
− HCHO

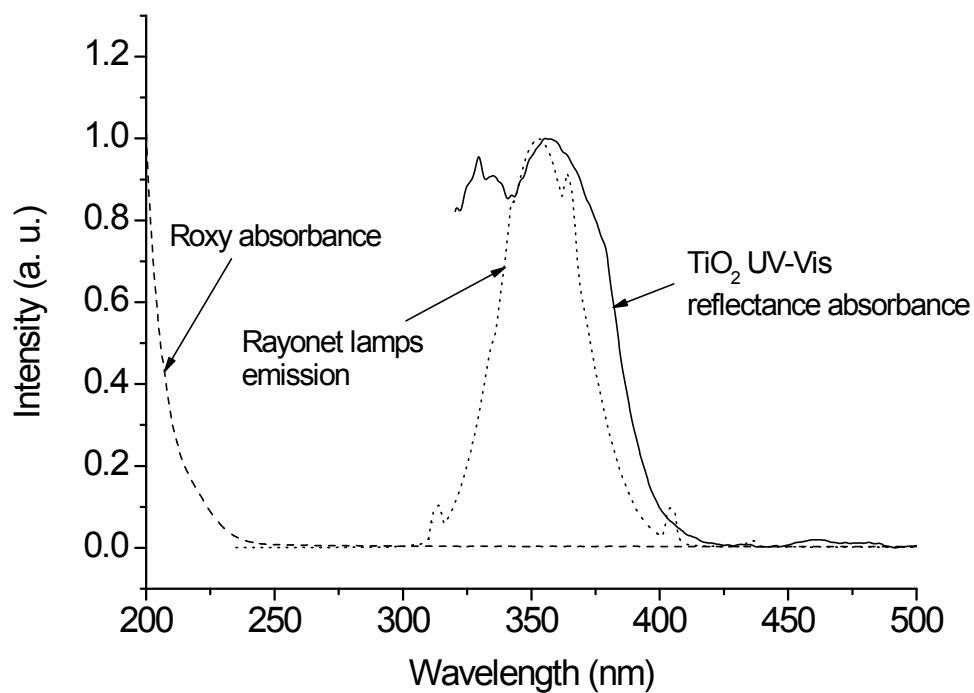m/z = 488.3   − H₂O   m/z = 470.3   − 72.1   m/z = 398.2

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Figure S1. PXRD diffractogram of the TiO₂ powder

Figure S2. Size distribution of TiO₂ particles dispersed in water found from the DLS measurement.

Figure S3. Normalized UV-Vis reflectance spectra of dry TiO$_2$ powder, 0.1 mg/ml Roxy solution in 0.1 M HCl, and the spectral distribution of the Rayonet lamps irradiation.