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Supplementary12 information to

# Rapid Screening of Antimalarial Drugs using Low-Temperature Plasma Desorption/Ionization Orbitrap Mass Spectrometry

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Table S 1: LTP-Orbitrap-MS parameters used fort the LTP-MS analysis.

| **MS scan parameters** | |
|---|---|
| Scan range | 50-550 |
| HCD gas | ON |
| Resolution | High |
| Polarity | Positive/negative |
| Lock masses | Off |
| Automatic gain control (AGC) | On |
| Maximum ion injection time | 100 ms |
| **MS source parameters** | |
| Sheath gas flow rate (L/hr) | 0 |
| Aux. gas flow rate (L/hr) | 0 |
| Sweep gas flow rate (L/hr) | 0 |
| Spray voltage (V) | 0 |
| Capillary voltage (V) | 35 |
| Capillary temperature (°C) | 300 |
| Tube lens voltage (V) | 100 |
| Skimmer voltage (V) | 20 |

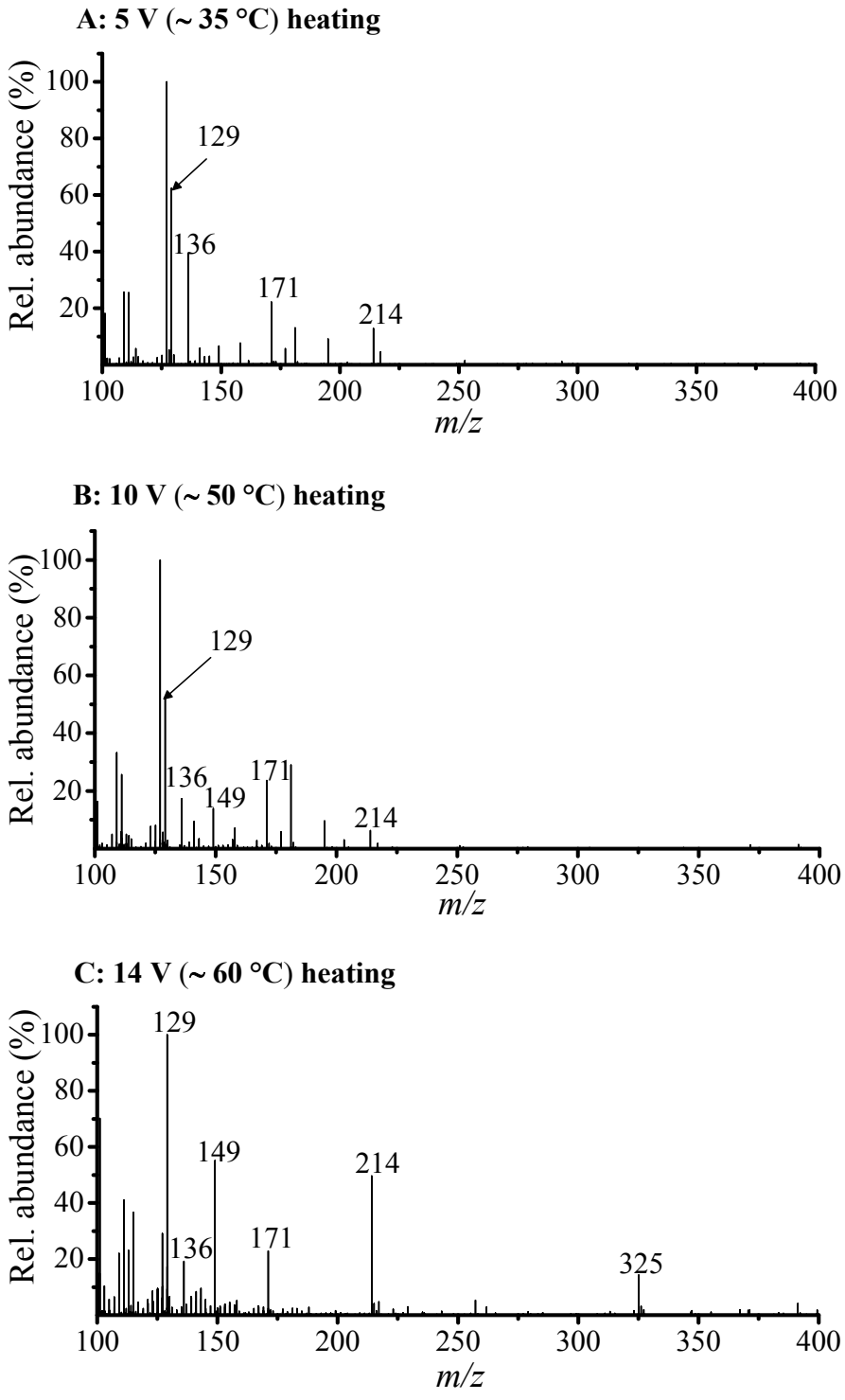


Figure S 1: Positive ion mode low-temperature plasma high-resolution mass spectrometry (LTP (+)-HR-MS) spectra of quinine with additional heating: A) 5.0 V (~35 °C) heating, B) 10.0 V (~50 °C) heating, and C) 14 V (~65 °C) heating Analyte: 10 µg/mL (30 ng absolute) of quinine (*m*/*z* 325.1916, $C_{20}H_{25}N_2O_2^+$).

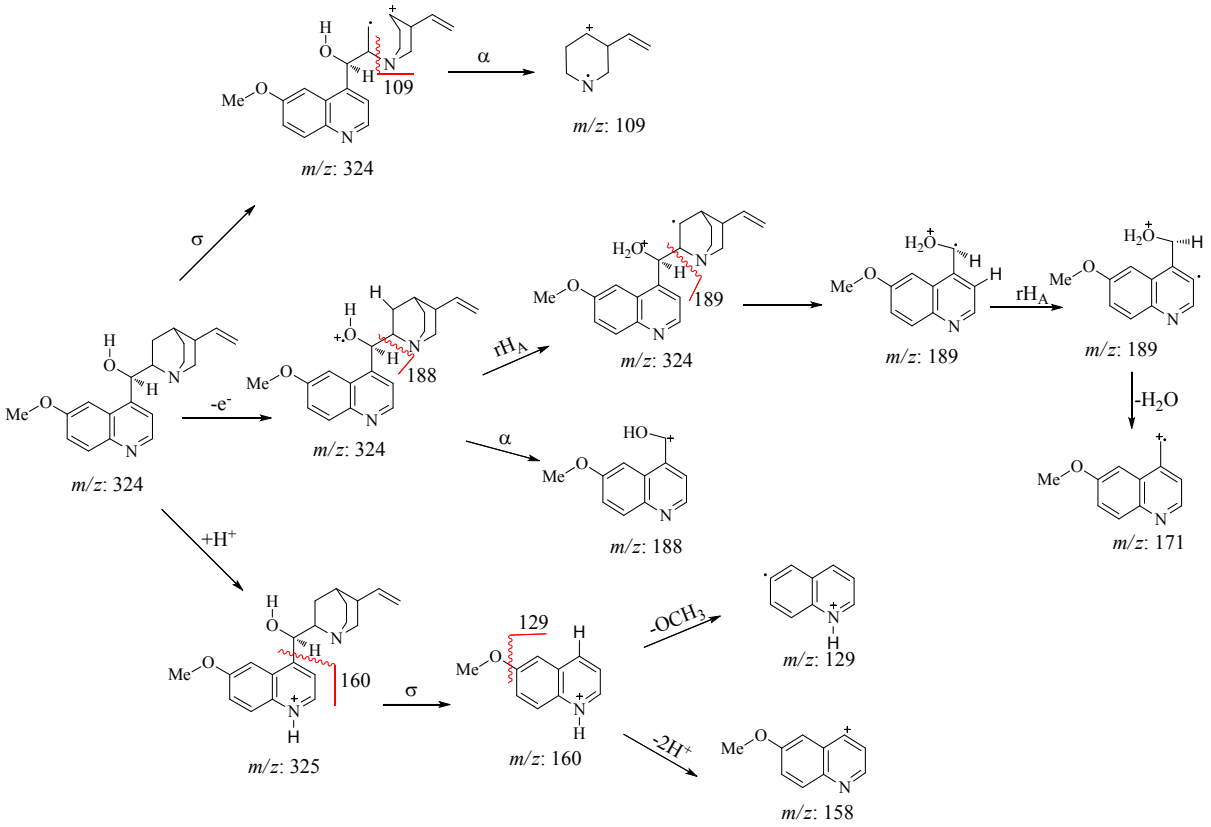


Figure S 2: Proposed fragmentation pathway of quinine showing the formation of free radical cations during LTP (+)-HR-MS analysis.

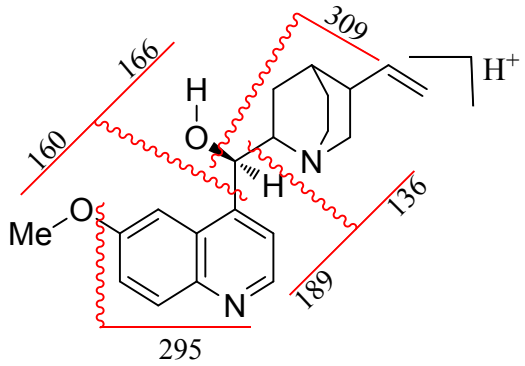


Figure S 3: Fragmentation pattern of the protonated molecule of quinine with known characteristic fragments as reported in literature.[1]

1 JEOL Mass Spectrometers, 2006, Tandem Mass Spectrometery (MS/MS), https://www.jeolusa.com/DesktopModules/Bring2mind/DMX/API/Entries/Download?EntryId=78&Command=Core_Download&language=en-US&PortalId=2&TabId=337, Acessed November 15th, 2018

Table S 2: Proposed fragment ions of quinine obtained with LTP (+)-HR-MS.

| Nominal mass (*m*/*z*) | Exact mass (*m*/*z*) | Relative mass accuracy (ppm) | Fragment ions | Source |
|---|---|---|---|---|
| 109 | 109.0891 | - | $C_7H_{11}N^{\bullet+}$ | Quinine |
| 129 | 129.0578 | - | $C_9H_7N^{\bullet+}$ | Quinine |
| 136 | 136.1124 | 2.3 | $C_9H_{14}N^+$ | Quinine |
| 149 | 149.0239 | 1.4 | $C_8H_5O_3^+$ | Phthalic anhydride |
| 160 | 160.0760 | 2.2 | $C_{10}H_{10}ON^+$ | Quinine |
| 166 | 166.1231 | 3.0 | $C_{10}H_{16}ON^+$ | Quinine |
| 171 | 171.0268 | -3.9 | $C_{11}H_9NO^{\bullet+}$ | Quinine |
| 188 | 188.0712 | -3.2 | $C_{11}H_{10}O_2N^+$ | Quinine |
| 325 | 325.1914 | -1.2 | $C_{20}H_{25}O_2N_2^+$ | Quinine |
| 341 | 341.1863 | 1.0 | $C_{20}H_{25}O_3N_2^+$ | Quinine oxide |
| 357 | 357.1812 | 1.0 | $C_{20}H_{25}O_4N_2^+$ | Quinine dioxide |
| 375 | 375.1920 | 1.5 | $C_{20}H_{25}O_5N_2^+$ | Quinine trioxide |

Table S 3: Proposed fragment ions of quinine obtained with LTP (+)-HR-MS with high-energy collision-induced dissociation (HCD) fragmentation

| Nominal mass (*m*/*z*) | Exact mass (*m*/*z*) | Relative mass accuracy (ppm) | Fragment ions | Source |
|---|---|---|---|---|
| 109 | 109.0891 | - | $C_7H_{11}N^{\bullet+}$ | Quinine |
| 129 | 129.0578 | - | $C_9H_7N^{\bullet+}$ | Quinine |
| 136 | 136.1124 | 2.6 | $C_9H_{14}N^+$ | Quinine |
| 149 | 149.0239 | 1.7 | $C_8H_5O_3^+$ | Phthalic anhydride |
| 160 | 160.0760 | 1.2 | $C_{10}H_{10}ON^+$ | Quinine |
| 166 | 166.1231 | 2.5 | $C_{10}H_{16}ON^+$ | Quinine |
| 171 | 171.0268 | -3.9 | $C_{11}H_9NO^{\bullet+}$ | Quinine |
| 188 | 188.0712 | -2.7 | $C_{11}H_{10}O_2N^+$ | Quinine |
| 325 | 325.1914 | -0.6 | $C_{20}H_{25}O_2N_2^+$ | Quinine |
| 341 | 341.1863 | 0.65 | $C_{20}H_{25}O_3N_2^+$ | Quinine oxide |
| 357 | 357.1812 | 0.75 | $C_{20}H_{25}O_4N_2^+$ | Quinine dioxide |
| 375 | 375.1920 | 0.88 | $C_{20}H_{25}O_5N_2^+$ | Quinine trioxide |

Table S 4: Compounds screened from drug tablet with their boiling point and vapour pressure.

| Compound | Boiling point (°C) [a] | Vapour pressure (mBar) [b] |
|---|---|---|
| Artemether | 357.5 ± 42.0 | $7.48 \times 10^{-5}$ |
| Lumefantrine | 642.0 ± 55.0 | $2.93 \times 10^{-17}$ |
| Atovaquone | 535.0 ± 50.0 | $3.76 \times 10^{-12}$ |
| Proguanil | 325.1 ± 44.0 | $3.15 \times 10^{-4}$ |

[a] Values calculated at 760 Torr (1013.24 mbar), [b] Calculated at 25 ° C

The values were obtained from https://scifinder.cas.org/scifinder, and were calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02 (© 1994-2017 ACD/Labs).

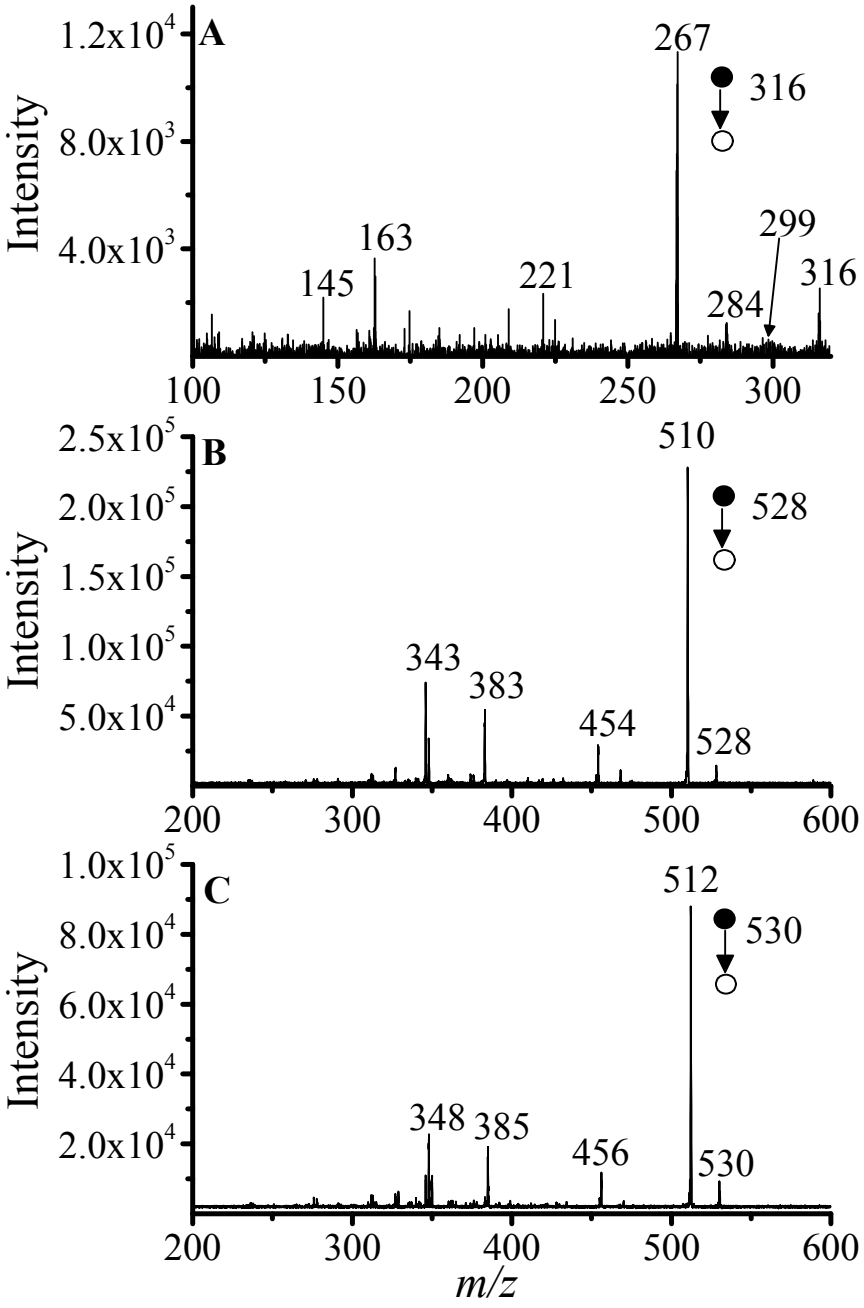


Figure S 4: ESI(+)-MS/MS spectra of the ammonium adduct of artemether ($C_{16}H_{26}O_5$) (A) at *m*/*z* 316, and the protonated molecular ion of lumefantrine ($C_{30}H_{32}Cl_3NO$) (B) at *m*/*z* 528 with, $^{35}Cl_3$ and (C) at *m*/*z* 530, with $^{35}Cl_2$ $^{37}Cl$.

Table S 5: Liquid chromatography triple quadrupole mass spectrometry (LC-QQQ-MS) parameters applied for the screening of artemether from Coartem drug tablet.

| **Scan parameters** | |
|---|---|
| Mass range | 100 - 420 |
| Scan duration (sec) | 3.00 |
| Inter scan delay (sec) | 0.15 |
| Ionization mode | ESI+ |
| Data type | Accurate mass |
| **ESI source** | |
| Capillary voltage (V) | 3.00 |
| Cone voltage (V) | 15.0 |
| Extractor voltage (V) | 5.0 |
| RF lens voltage (V) | 5.0 |
| Source block temp. (°C) | 100 |
| Desolvation temp (°C) | 400 |
| Analyser vacuum (mBar) | $6.8 \times 10^{-6}$ |
| Gas cell vacuum (mBar) | $2.0 \times 10^{-5}$ |
| Nebulizer gas flow (L/hr) | 68.0 |
| Desolvation gas flow (L/hr) | 636.0 |

Table S 6: LC-QQQ-MS parameters used for the screening of lumefantrine from Coartem drug tablet.

| **Scan parameters** | |
|---|---|
| Mass range | 200 - 600 |
| Scan duration (sec) | 3.00 |
| Inter scan delay (sec) | 0.15 |
| Ionization mode | ESI+ |
| Data type | Accurate mass |
| **ESI source** | |
| Capillary voltage (V) | 3.00 |
| Cone voltage (V) | 60.0 |
| Extractor voltage (V) | 5.0 |
| RF lens voltage (V) | 5.0 |
| Source block temp. (°C) | 100 |
| Desolvation temp (°C) | 400 |
| Analyser vacuum (mBar) | $6.8 \times 10^{-6}$ |
| Gas cell vacuum (mBar) | $2.0 \times 10^{-5}$ |
| Nebulizer gas flow (L/hr) | 68.0 |
| Desolvation gas flow (L/hr) | 636.0 |