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Test purchase, synthesis, and characterization of 2-methoxydiphenidine (MXP) and differentiation from its meta- and para-substituted isomers

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Test purchase, synthesis and characterization of 2-methoxydiphenidine (MXP) and differentiation from its meta- and para-substituted isomers

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\[\begin{align*}
2-\text{MXP} & : & (2-\text{MeO-diphenidine}) \\
3-\text{MXP} & : & \text{3-MXP} \\
4-\text{MXP} & : & \text{4-MXP}
\end{align*}\]
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GC-EI-quadrupole mass spectra obtained from all three synthesized MXP isomers

Agilent 6980 GC coupled to an Agilent 5973 MSD (HP-5ms column, 30 m x 0.25 mm x 0.25 pm). Helium carrier gas at a constant flow of 1 mL/min in splitless mode. Injection port and transfer line set at 250 °C and 280 °C. Oven temperature: 40 °C held for 1 min, ramped at 12 °C/min to 280 °C, held for 5 minutes, then ramped again at 20 °C/min to 300 °C and held for 3 min. The total run time was 30 min.
HPLC-SIM-MS traces of powdered 2-MXP sample s vs. synthesized standards

3-MXP: 21.193 min
4-MXP: 21.738 min
2-MXP: 23.403 min
ESI-QqQ-MS/MS of synthesized MXP isomers

2-MXP MRM R  68 (0.686) Cn (Cen,2, 80.00, Ht); Cm (1:197)

Product ions of 296ES+
2.10e7

3-MXP MRM R  133 (1.342) Cn (Cen,2, 80.00, Ht); Sm (SG, 2x1.00); Cm (1:197)

Product ions of 296ES+
2.72e7

4-MXP MRM R  137 (1.382) Cn (Cen,2, 80.00, Ht); Sm (SG, 2x1.00); Cm (2:198)

Product ions of 296ES+
2.77e7

ESI-QqQ-MS/MS of synthesized MXP isomers
Drug Testing and Analysis – McLaughlin et al. – Supplementary data

UHPLC-ESI-QTOF-MS/MS of synthesized MXP isomers
**Rf values:**
2-MXP: 0.57
3-MXP: 0.77
4-MXP: 0.60

Mobile phase: CH₂Cl₂/CH₃OH (9:1) and 0.8% NH₄OH (7N in CH₃OH)
Stationary phase: TLC Silica gel 60 F₂₅₄ 10 x 10 cm
Detection: A) UV (254 nm); B) modified Dragendorff Ludy-Tenger reagent.
Bismuth subcarbonate (1 g), potassium iodide (6 g) and concentrated hydrochloric acid (15 mL) were diluted with water to give a final volume of 100 mL.

TLC analysis of powdered 2-MXP samples vs. synthesized standards
MAII Orbitrap mass spectrum obtained from 2-MXP tablet with \([\text{M} + \text{H}]^+\) at \(m/z\) 296.2009 using 3-nitrobenzonitrile as matrix. Insert: observed \(m/z\) 296.2009 peak (top); theoretical \(m/z\) value of 2-MXP (bottom).

MAII Orbitrap mass spectrum obtained from synthesized 2-MXP HCl standard (100 ppb) with \([\text{M}+\text{H}]^+\) at \(m/z\) 296.2008 using 3-nitrobenzonitrile as matrix. Insert: observed \(m/z\) 296.2008 peak (top); theoretical \(m/z\) value of 2-MXP (bottom).

Matrix assisted inlet ionization mass spectra of 2-MXP tablet vs. 2-MXP standard
Drug Testing and Analysis – McLaughlin et al. – Supplementary data

\[ ^1H\text{-NMR, 400 MHz, free base, } CDCl_3 \]

2-MXP tablet extract

Synthesized 2-MXP standard

Synthesized 3-MXP standard

Synthesized 4-MXP standard

\[ ^1H\text{-NMR of 2-MXP extracted from tablet vs. MXP isomers} \]
$^{13}$C-NMR of 2-MXP extracted from tablet vs. MXP isomers

$^{13}$C-NMR, 100 MHz, free base, CDCl$_3$
ATR-FT-IR spectra of three MXP isomers

2-MXP HCl
Drug Testing and Analysis – McLaughlin et al. – Supplementary data

3-MXP HCl

%T
45.0 50.0 55.0 60.0 65.0 70.0 75.0 80.0 85.0 90.0 95.0 98.1
4000.0 3600 3200 2800 2400 2000 1800 1600 1400 1200 1000 800 600 400.0
3027.62 2942.03 2850.19 2800.19 2598.67 2520.51 2426.12 2373.85 1592.83 1493.72 1480.27 1466.54 1451.08 1298.35 1238.09 1203.02 1154.79 1171.91 1117.91 1097.00 1007.00 981.75 935.78 899.28 873.78 851.84 802.74 761.51 729.85 707.49 681.84 620.51 583.68 557.22 532.92 510.53 cm⁻¹

References: