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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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Agilent 6980 GC coupled to an Agilent 5973 MSD (HP-5ms column, 30 m x 0.25 mm x 0.25 µm). 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

m/z 296
50 V
ESI-QqQ-MS/MS of synthesized MXP isomers

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

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

4-MXP MRM R  137 (1.382) Cn (Cen,2, 80.00, Ht); Sm (SG, 2x1.00); Cm (2:198)
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: CH$_2$Cl$_2$/CH$_3$OH (9:1) and 0.8% NH$_4$OH (7N in CH$_3$OH)

Stationary phase: TLC Silica gel 60 F$_{254}$ 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 [M + 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 [M+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

$^1$H-NMR of 2-MXP extracted from tablet vs. MXP isomers

$^1$H-NMR, 400 MHz, free base, CDCl$_3$

2-MXP tablet extract

Synthesized 2-MXP standard

Synthesized 3-MXP standard

Synthesized 4-MXP standard

$^1$H-NMR of 2-MXP extracted from tablet vs. MXP isomers
Supplementary data

$^{13}$C-NMR of 2-MXP extracted from tablet vs. MXP isomers

$^{13}$C-NMR, 100 MHz, free base, CDCl$_3$