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Prevalence of cocaine adulterant tetramisole in hair and seized cocaine samples

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1. Background & Aims

• Not only the anthelmintic levamisole (*S*-PTHIT) is used as adulterant for cocaine but also the racemic form tetramisole (*S*-/*R*-PTHIT) was recently detected in seized cocaine

***S*-/*R*-Phenyltetrahydroimidazothiazol, PTHIT**

Tetramisole (racemate)

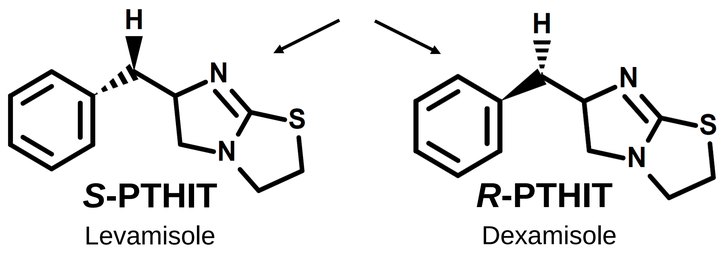

Fig.1: Chemical structures of PTHIT stereoisomers levamisole (*S*-PTHIT) and dexamisole (*R*-PTHIT)

• To monitor the prevalence of PTHIT in cocaine-positive hair samples

• To distinguish PTHIT stereoisomers in hair and seized street cocaine samples

2. Methods

2.1 Cocaine-positive hair samples

a. Routine samples from 03/2017-02/2018 (mainly 2017)
cocaine > 500 pg/mg (SoHT cut-off); n= 327

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Achiral LC-MS/MS analysis for *S*-/*R*-PTHIT

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positive for *S*-/*R*-PTHIT (> 2.5 pg/mg hair): n = 271 (83 %)
S-/*R*-PTHIT > 1'000 pg/mg hair: n= 64 (20 %)

b. Routine samples from mainly 2017
S-/*R*-PTHIT > 1'000 pg/mg hair, n= 64

⬇

Chiral LC-MS/MS analysis for levamisole (*S*-PTHIT) & dexamisole (*R*-PTHIT)

2.2 Seized street cocaine samples

Samples seized from 2013 - 2016 in the Canton of Zurich
cocaine positive & *S*-/*R*-PTHIT positive; n= 24

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Chiral LC-MS/MS analysis for levamisole (*S*-PTHIT) & dexamisole (*R*-PTHIT)

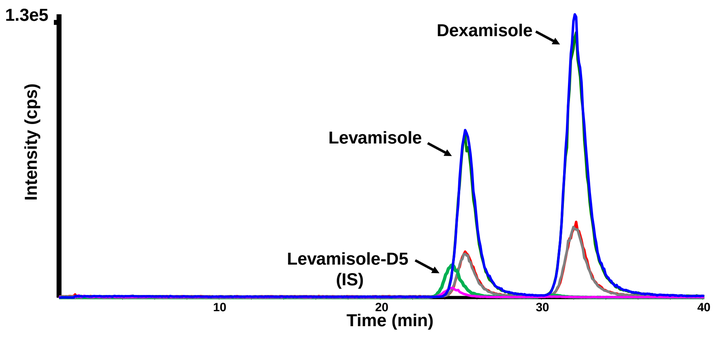

Fig.2: Chiral LC-MS/MS chromatogram of levamisole/ dexamisole and the internal standard (IS) levamisole-D5; analyte separation on a chiral AGP column (100 mm x 4 mm, 5 µm).

Contact

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Conclusion

- Strong prevalence of PTHIT stereoisomers in cocaine-positive hair samples
- Enantiomeric ratios of *S*-/*R*-PTHIT in hair below 1 are surprising in light of the strong prevalence of tetramisole in seized cocaine samples
- Higher dexamisole than levamisole concentrations in hair most probably arise from stereoselective metabolism and/or elimination in the body
- Important findings in light of the different pharmacological activities of the stereoisomers, and, hence, potentially different adverse effects
- Presence of PTHIT stereoisomers in biological samples may have hitherto been underestimated
- Toxicological findings in intoxication cases with adulterated cocaine should consider levamisole and dexamisole

3. Results

3a. Hair samples positive for cocaine and *S*-/*R*-PTHIT, n= 271 out of 327 (83 %)

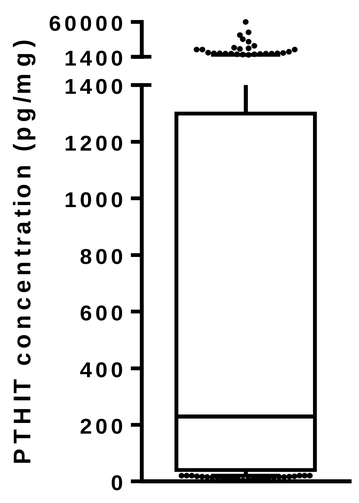

Fig.3: PTHIT concentrations in cocaine-positive hair samples from mainly 2017, n= 271 out of 327 (83 %); 10th-90th percentile box-and-whiskers plot.

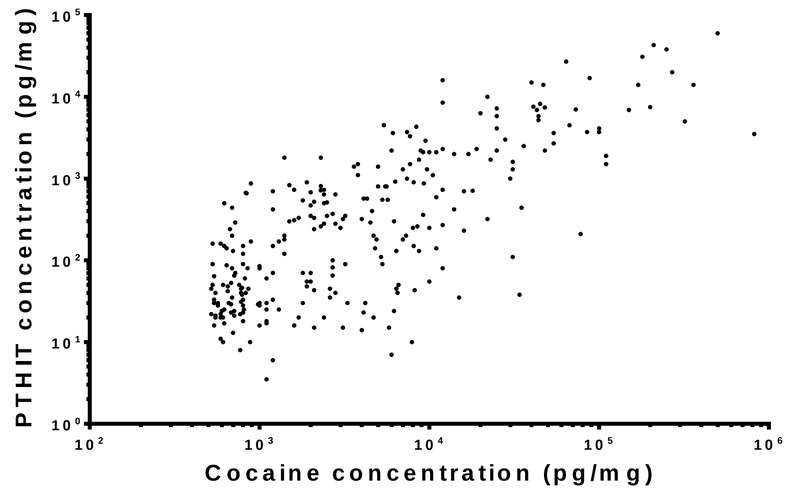

Fig.4: Correlation of PTHIT and cocaine concentrations in hair samples from mainly 2017. Statistics: Spearman r= 0.7092, p<0.0001.

- **Strong prevalence of *S*-/*R*-PTHIT in cocaine-positive hair samples with *S*-/*R*-PTHIT concentrations ranging from 2.5 to approximately 60'000 pg/mg hair**
- ***S*-/*R*-PTHIT and cocaine concentrations are positively correlated**

3b. Enantiomeric ratios in hair and seized street cocaine samples

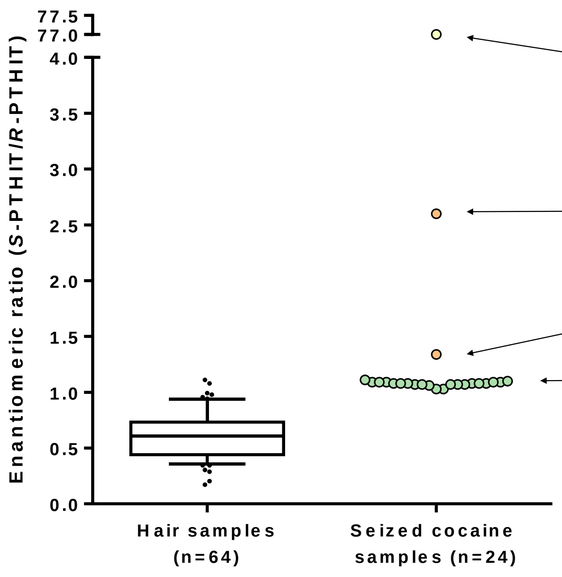

Fig.5: Enantiomeric ratios of levamisole/dexamisole in cocaine users' hair samples with a PTHIT concentration > 1'000 pg/mg (10th-90th percentile box-and-whiskers plot) and cocaine samples seized from 2013 - 2016.

3c. Seized street cocaine samples from 2013 - 2016, n= 24

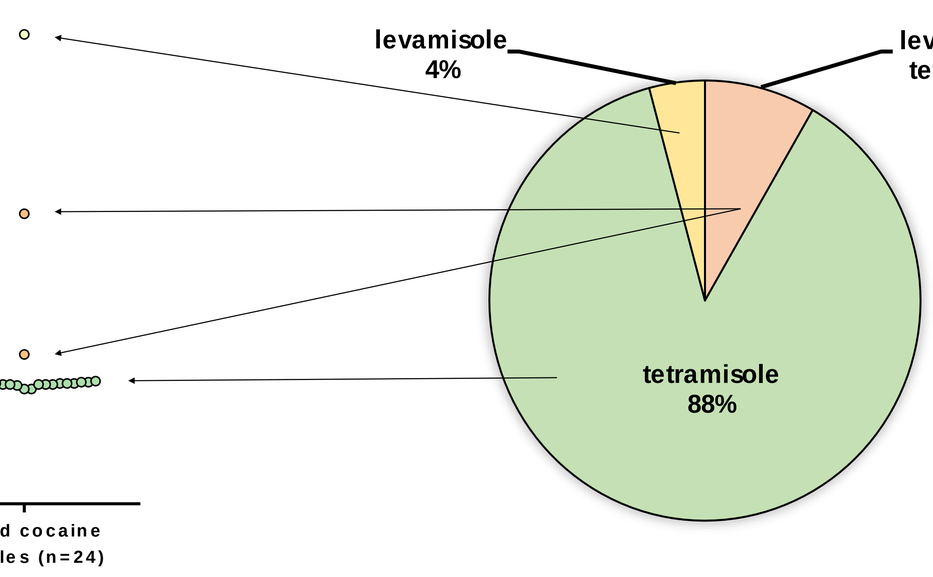

Fig.6: Percentages of levamisole, tetramisole and non-racemic PTHIT (tetramisole + levamisole) of investigated street cocaine samples seized in the Canton of Zurich, Switzerland.

- **All hair samples positive for levamisole (*S*-PTHIT) and dexamisole (*R*-PTHIT)**
- **Enantiomeric ratios of *S*-/*R*-PTHIT (levamisole/dexamisole) in hair mainly below 1 (median: 0.61)**
- **Seized cocaine mainly contained tetramisole; only one sample positive for levamisole only and only two samples contained non-racemic mixtures of PTHIT, potentially due to adulteration with tetramisole and levamisole**

Reference

Milena M. Madry, Thomas Kraemer, Markus Baumgartner (2018) Cocaine adulteration with the anthelmintic tetramisole (levamisole/dexamisole): long-term monitoring of its consumption by chiral LC-MS/MS hair analysis (submitted)