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Letter to the Editor

Sildenafil analogs used for adulterating marihuana

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Dear Sir,

In recent years marihuana was found adulterated with powdered glass or chalk [1–3]. The adulterants adhered to the naturally excreted resin making it the marihuana look like being of a higher quality. Earlier this year in Germany elemental lead had been used as an adulterant to increase weight, causing symptoms of poisoning in at least 100 marihuana smokers [4]. Because of the health risk adulterants may pose marihuana is regularly checked in The Netherlands for the presence of adulterants.

We report here a case study where two liquids used for adulterating marihuana were investigated for the presence of adulterants. Samples A and B were provided to our laboratory in plastic screw-capped container and without any further description. Standard analysis using HPLC–DAD–MSⁿ and direct infusion

MSⁿ revealed the presence of a carbohydrate in sample A and the presence of two illegal analogs of sildenafil (Viagra[®]) in Sample B (Fig. 1). The illegal erectogenics were identified as a mixture of thio-homosildenafil (THS) and its chemical precursor homosildenafil (HS) in a 10:1 ratio, using a method described by our laboratory earlier [5,6]. In addition, traces of several related chemical structures were detected but these were not identified further. Reference standards had been isolated from adulterated dietary supplements in previous investigations [5,6].

A crude smoking experiment confirmed that THS, HS and reference sildenafil citrate could be inhaled by smoking. For this experiment, a portion of Sample B was evaporated leaving a white powder. Cigarettes were prepared using 1.2 g of hand-rolling tobacco to which was added the arbitrary amount of 15 mg of sildenafil citrate or THS/HS powder. Cigarettes were mounted on a gas-washing bottle filled with 300 ml of MeOH and a gentle vacuum was applied allowing the cigarette to burn at a rate of approximately 1 cm/min. After the cigarette had burned for 5 min, the MeOH solution was analyzed by HPLC–MSⁿ using selected reaction monitoring (sildenafil: m/z 475 → 377; HS: m/z 489 → 461 and THS m/z 505 → 355) [6]. For chromatographic separation 5 μ l was injected on a Waters Symmetry C₁₈ column (2.1 mm × 100 mm, 3.1 μ m) held at 30 °C using Solvent A–0.1% (v/v) formic acid in ACN and Solvent B–0.1% (v/v) formic acid in H₂O: 0–20 min gradient elution from A/B = 5/95 to 90/10, 20–25 min isocratic A/B = 90/10, 25–30 min: isocratic A/B = 5/95.

Both THS and HS are phosphodiesterase 5 (PDE-5) inhibitors like sildenafil (Viagra[®]) and so far were identified in illegal

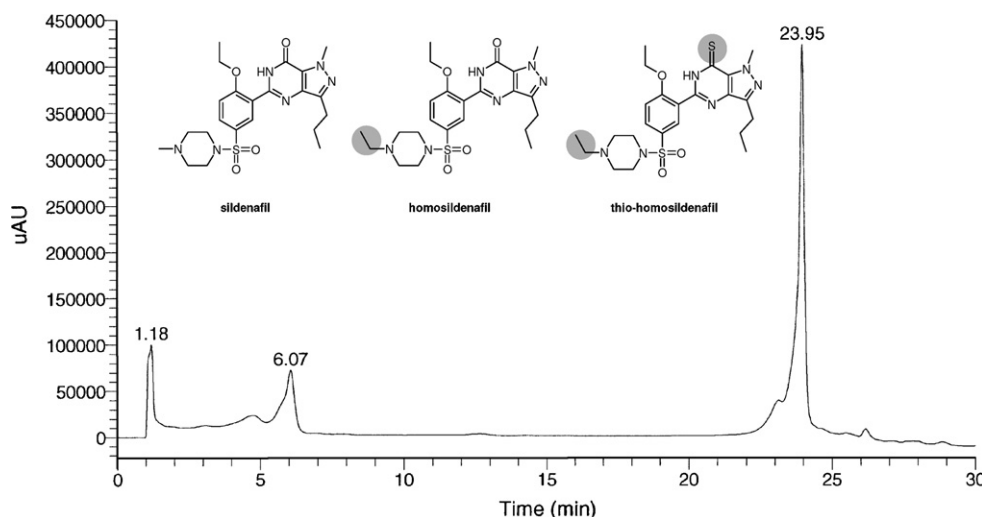


Fig. 1. UV chromatogram of the suspicious liquid with homosildenafil ($RT = 6.07$) and thio-homosildenafil ($RT = 23.95$). The grey areas indicate the differences in chemical structure from sildenafil.

erectogenics only. The effect a PDE-5 inhibitor would exert on lung tissue is well described in literature. In patients suffering from pulmonary hypertension orally administered sildenafil (Revatio®) causes pulmonary vasodilatation improving their breathing [7–9]. No reports on smoking of PDE-5 inhibitors could be found in literature, but inhalation of nebulized sildenafil is reportedly effective in animal studies [10,11].

Assuming marihuana is adulterated with PDE-5 inhibitors for a specific reason the adulterators may aim at evoking drug–drug interactions. Though interactions studies were not found in literature a recent US study showed a strong association between males smoking marijuana and taking un-prescribed sildenafil tablets [12]. The investigators suggest sildenafil may be used to counter marijuana-induced loss of libido. Still, in our case, this does provide a solid rationale for smoking marihuana with a PDE-5 inhibitor unless the objective is to keep buyers unaware.

As this is the first and only case there is the possibility of an isolated incident. However, since PDE-5 inhibitor could have an effect it may still be not coincidental. A possible explanation that should be investigated is whether an interaction could arise resulting in the increased uptake of psychoactive components from marihuana smoke, enhancing the experience. Such a study would contribute to the understanding and health risks of the concomitant use of marihuana and PDE-5 inhibitors.

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