D5 UPLC-MS/MS for the Screening, Confirmation, and Quantification of Illegal Drugs Added to Herbal/Dietary Supplements for the Enhancement of Male Sexual Performance

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The goals of this presentation are: (1) to provide insight into the global problem of the adulteration of herbal and dietary supplements with erectile dysfunction (ED) drugs; (2) detail their synthetic analogues; and, (3) to present a validated method for these compounds.

This presentation will impact the forensic science community by providing a new method for the simultaneous analysis of >30 ED drugs and their analogues.

The adulteration of herbal/dietary supplements with erectile dysfunction (ED) drugs and their analogues is reported worldwide and is an increasing problem.[1,2] The sale of so-called 100%, "all-natural" products has become a highly profitable business for online pharmacies; however, these products can pose a serious threat to consumers due to the undisclosed presence of approved/prescription drugs or the unknown safety and toxicity profile of unapproved ED drugs. Government authorities play a crucial role in the control of these products for the safety of human health. The Drug QC Laboratory in Qatar, has been involved in the testing of adulterated and counterfeit products for a number of years.[3] The goal of this study was to develop an analytical procedure for herbal and dietary products that are marketed to improve male sexual performance and imported to Qatar.

A simple and rapid Ultra Performance Liquid Chromatography-Tandem Mass Spectrometry (UPLC-MS/MS) procedure for the analysis of >30 synthetic chemicals in herbals without sample cleanup is presented. A spectral library for synthetic compounds (including 28 ED drugs and their analogues) was generated from reference standards for automated routine sample screening. Full scan MS analysis was performed simultaneously in both positive and in high energy negative Electrospray Ionization modes (ESI); the latter function permitted the detection of new, unknown ED analogues by generation of common, high intensity fragment ions at m/z 282, 298, and 232. In addition, a highly sensitive and selective MS/MS method was developed for confirmation and quantification using two multiple reaction monitoring (MRM) transitions for each compound. This method was validated for three different matrices (capsules/tablets/pills, honey, and herbal drink). Calibration curves (0.2ng/mL – 1000ng/mL) were prepared both in the absence and presence of matrix. The limit of quantification was 0.5ng/mL for most compounds based on a signal-to-noise ratio of ≥10:1 for both quantifier and qualifier ions and with %CV reported less than 11% for 29 compounds spiked in herbal matrices at 2ng/mL. The developed method was applied to 43 suspected dietary products that had been imported into Qatar during 2010 and 2011. The samples were received from customs, herbal registration section and clearance section of health authorities, and analyzed by the developed procedure. A total of 18 products were found to be adulterated: 11 with sildenafil, two with thiodimethyl-sildenafil and five found to contain a combination of yohimbine, tadalafil, aminotadalafil, dimethylsildenafil, and thiosildenafil.

Reference:

1. Tainted Sexual Enhancement Products, http://www.fda.gov/Drugs/ ResourcesForYou/Consumers/BuyingUsingMedicineSafely/ MedicationHealthFraud/ucm234539.htm
2. Hidden Risks of Erectile Dysfunction "Treatments" SoldOnline, http://www.fda.gov/ForConsumers/ConsumerUpdates/ ucm048386.htm
3. Dubai raid nets Dh70m worth of fake Viagra, http://www.thenational.ae/news/uae-news/dubai-raid-nets-dh70m- worth-of-fake-viagra

ED Analogues, Herbal/Dietary Supplements, UPLC-MS/MS

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