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ORIGINAL RESEARCH

Cross-Sectional Survey of Adulterated Sexual Enhancement Products Sold in the Sacramento Area of California

Tessa Fischer[1,2], Jenna Tucker[1,2], Charlie Li[3], Kyungmi Min[3], Dadong Xu[3], Laurence R Upjohn[1], Madhur Kumar[1]

[1]Food and Drug Branch, California Department of Public Health, Sacramento, CA, USA; [2]California Epidemiologic Investigation Service (Cal EIS) Fellowship Program, California Department of Public Health, Sacramento, CA, USA; [3]Food and Drug Laboratory Branch, California Department of Public Health, Richmond, CA, USA

Correspondence: Madhur Kumar, Food and Drug Branch, California Department of Public Health, 1500 Capitol Avenue, MS 7602, Sacramento, CA, 95814, USA, Email madhur.kumar@cdph.ca.gov

Purpose: The Food and Drug Administration (FDA) has warned against tainted products for sexual enhancement containing prescription phosphodiesterase-5 (PDE5) inhibitors marketed as dietary supplements. The California Department of Public Health (CDPH)'s Food and Drug Branch (FDB) initiated a study to assess the presence of such adulterated products, specifically to identify the presence of PDE5 inhibitors in dietary supplements marketed for sexual enhancement, sampled at local retail locations.

Methods: A convenience sample of products marketed as sexual enhancement dietary supplements was purchased from retail stores, within a 15-mile radius of downtown Sacramento, California. Samples were submitted to the Food and Drug Laboratory Branch (FDLB) and screened for 19 different PDE5 inhibitors using liquid chromatography-mass spectrometry. Samples were collected and analyzed from 2016 to 2018.

Results: One hundred and two different products were purchased from 28 different retail locations. Sixty-seven percent were found to be adulterated with at least one PDE5 inhibitor. Of the positive samples, 40% were found to contain one PDE5 inhibitor and 60% were found to contain two or more. Sildenafil was the most common PDE5 inhibitor identified (74%), followed by tadalafil (59%). Eighteen percent of the tested samples had been associated with previous FDA warnings listed in their Tainted Products Database. Of these warning-associated samples, 72% were found to contain PDE5 inhibitors and 46% of these contained at least one of the same adulterants reported by the FDA.

Conclusion: FDA reports and warnings have focused on dietary supplements found online or through screenings of international mail shipments. FDB results add to FDA findings by demonstrating that such adulterated products marketed for sexual enhancement are also sold at retail locations in California. These products have the potential to cause severe adverse health effects and therefore, it is essential to raise awareness of this significant public health concern.

Keywords: dietary supplements, sexual enhancement products, adulteration

Introduction

In the US, dietary supplements (DS) are not subject to pre-market approval for safety and efficacy by the FDA.[1] Post-market surveillance by the FDA has found increasing numbers of supplements to be adulterated or tainted, meaning that they contain undeclared or hidden, unapproved drug ingredients.[2,3] These hidden ingredients have the potential to cause serious adverse health effects.

The Food and Drug Branch (FDB) of the California Department of Public Health (CDPH) is charged with ensuring that DS manufactured and/or sold in California (CA) are safe for consumption and are not mislabeled or adulterated. FDB initiated efforts to assess the presence of adulterated DS sold in retail stores in the Greater Sacramento area of CA. This study was designed to duplicate the consumer experience and further investigate what FDA has reported on a national level; thus, it does not represent

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regulatory or enforcement-related activity. The FDA's Tainted Products Marketed as Dietary Supplements Database, now the Health Fraud Product Database, lists products that have been associated with previous warnings.[4] These warnings include warning letters, online advisory letters, recalls, public notifications, and press announcements for issues varying from products marketed as dietary supplements claiming to cure, mitigate, treat or prevent disease, to the use of undeclared ingredients or new dietary ingredients.[4]

Review of FDA's Tainted Products Marketed as Dietary Supplements Database shows that products marketed for sexual enhancement represent the largest category reported to be adulterated with hidden pharmaceutical drug ingredients.[3] This category of DS is most commonly found to be adulterated or tainted with phosphodiesterase-5 (PDE5) inhibitors, which are the class of drugs prescribed to treat erectile dysfunction (ED).[3,5] PDE5 inhibitors commonly prescribed to treat ED include sildenafil, tadalafil, and vardenafil.[5] Eighty PDE5 inhibitor analogues have been identified as adulterants in DS.[6] PDE5 inhibitors are contraindicated in people who take medications containing nitrates, which are commonly prescribed for heart disease.[7] These drug interactions have the potential to lower blood pressure to a dangerous level and can lead to fatal cardiovascular collapse.[7] PDE5 inhibitor adulteration in sexual enhancement DS is a world-wide problem.[8–13] Ten out of 64 sexual enhancement DS samples collected from a Czech marketplace from 2009 to 2015 were found to have PDE5 inhibitor adulterants and 34 out of 62 DS for sexual enhancement were found to be adulterated with at least one PDE5 inhibitor from a Malaysian market from 2014 to 2016.[8,9] Other published studies also emphasize the global nature of this public health challenge.[10–13]

This cross-sectional survey study focuses on testing for the presence of prescription PDE5 inhibitors and/or 16 of their analogues in products marketed as DS for sexual enhancement, available at retail locations in the Sacramento area of California, with particular interest in some products that had received previous FDA warnings.

Materials and Methods

A convenience sample of 102 different products marketed as DS for sexual enhancement was purchased by FDB staff from gas stations, corner markets, liquor/cigarette stores, health/nutrition stores, and pharmacies within a 15-mile radius of downtown Sacramento, CA, between September 2016 and November 2017. Sampling was subject to a number of logistical considerations, such as ease of access to locations and prioritizing high traffic locations, laboratory testing schedules, availability of sexual enhancement products at visited locations, and funding availability for sample purchasing; thus, sampling was not completely randomized, and locations sampled were not evenly distributed throughout the collection area. Products were selected based on which of those marketed for sexual enhancement were available/visible at the retail locations on the day they were visited, replicating an average consumer experience, and present in quantities sufficient for laboratory testing. When feasible, interest in FDA's warnings targeted some of the sampling toward products named in the FDA's Tainted Products Marketed as Dietary Supplements Database.[4]

Only products that were marketed in a dry pill/tablet form were tested, except for one product that was sold as an encapsulated liquid. Each sample included at least three pills/tablets of a single product for analysis. Some locations had less than three pills of a given product in stock; in these cases, the same product was purchased from more than one location, ensuring that lot codes and expiration dates remained the same. For each product sampled, the following information was recorded: product name, retail location, FDA warning(s) associated with the product (if applicable), packaging unit (single-pill blister pack or pill bottle), and packaging language as available (warnings, ingredients, country of origin, and manufacturer/distributor information).

Samples were collected and submitted to the CDPH Food and Drug Laboratory Branch (FDLB) for analysis. A 50 mg sample was utilized for sample preparation and extraction. A qualitatively spiking sample was prepared by spiking each 200ul of stock solutions (sildenafil, vardenafil, and tadalafil, each 500 ppm) before analysis by liquid chromatography mass spectrometry (LC/MS). FDLB screened for 19 different PDE5 inhibitors using LC/MS, following methods previously described by the FDA's Forensic Chemistry Center (Table 1).[14] Ultra-performance liquid chromatography-ion trap mass spectrometry (UPLC/MS) was utilized for the separation, detection, and confirmation of ED drugs in dietary supplement samples.[14] This process is designed to detect these analytes at concentrations from 0.5 μg/mL to 5 μg/mL in the final extraction solutions depending on compounds.[14] Tandem mass spectrometry capabilities were utilized to distinguish between compounds having the same nominal mass and/or formula, as many of the analytes for which FDLB screened are structurally similar.[14] The concentrations of the detected PDE5 inhibitors were estimated in the adulterated samples. This was done by comparing the analyte peak area in a sample to that of the

Table 1 Phosphodiesterase-5 (PDE5) Inhibitors Included in LC-MS Screen

PDE5 Inhibitor	Formula
Acetildenafil (hongdenafil)	$C_{25}H_{34}N_6O_3$
Aminotadalafil	$C_{21}H_{18}N_4O_4$
Dimethylsildenafil (aildenafil, methisosildenafil)	$C_{23}H_{32}N_6O_4S$
Gendenafil	$C_{19}H_{22}N_4O_3$
Homosildenafil	$C_{23}H_{32}N_6O_4S$
Hydroxyacetildenafil (hydroxyhongdenafil)	$C_{25}H_{34}N_6O_4$
Hydroxyhomosildenafil	$C_{23}H_{32}N_6O_5S$
Hydroxythiohomosildenafil (hydroxyhomosildenafil thione, sulfohydroxyhomosildenafil)	$C_{23}H_{32}N_6O_4S_2$
N-Desethyl vardenafil	$C_{21}H_{28}N_6O_4S$
N-Desmethyl sildenafil	$C_{21}H_{28}N_6O_4S$
Norneosildenafil	$C_{22}H_{29}N_5O_4S$
Pseudovardenafil (piperadino vardenafil, piperidenafil)	$C_{22}H_{29}N_5O_4S$
Sildenafil	$C_{22}H_{30}N_6O_4S$
Tadalafil	$C_{22}H_{19}N_3O_4$
Thiodimethyl sildenafil (thioaildenafil, sulfoaildenafil)	$C_{23}H_{32}N_6O_3S_2$
Thiohomosildenafil (homosildenafil thione, sulfohomosildenafil)	$C_{23}H_{32}N_6O_3S_2$
Thiosildenafil (sildenafil thione, sulfosildenafil)	$C_{22}H_{30}N_6O_3S_2$
Vardenafil	$C_{23}H_{32}N_6O_4S$
Xanthoanthrafil (benzamidenafil)	$C_{19}H_{23}N_3O_6$

corresponding standard and multiplying this by the dilution factor, which was 2000. For example, if the peak area of sildenafil in a sample is 100 and is 50 in a 1 ppm standard, the estimated concentration of sildenafil in the actual sample would be (100 ÷ 50) x 1 ppm x 2000 = 4000 ppm.

Descriptive statistical analyses were performed using SAS Enterprise Guide, version 7.1 (SAS Institute) and Microsoft Excel 2010 for Windows (Microsoft Inc). Statistical significance was determined using a p-value of 0.05 and/or a 95% confidence interval (CI) that contains the odds ratio (OR) value and does not contain the null value. When PDE5 inhibitors were detected in a tested product, the concentrations of the identified drug ingredients were semi-quantified for the adulterated sample followed by dosage estimate. This process has been used in multiple studies for concentration estimates.[15,16]

Results

One hundred and two different sexual enhancement product samples were purchased between September 2016 and November 2017 and sent to the FDLB laboratory for analyses. Laboratory results showed that 67% (68/102) of the samples were adulterated with at least one PDE5 inhibitor. The sample products, marketed as dietary supplements, were purchased from 28 different retail locations which included both small and large stores, within a 15-mile radius of downtown Sacramento, CA. Eighty-eight percent (66/75) of samples purchased from smaller retail locations like gas stations, liquor stores, cigarette shops or mini marts were found to be adulterated while only 7% (2/27) of samples purchased from larger retail locations like pharmacies, health and nutrition stores or supermarkets were found to be adulterated.

Of the positive samples, 40% (27/68) were found to contain one, 49% (33/68) were found to contain two, 9% (6/68) were found to contain three, and 3% (2/68) were found to contain four (Table 2) of the 19 compounds screened for in the

Table 2 Number of Adulterants Detected in the 2016 – 2017 Survey of Products That Were Marketed as Dietary Supplements for Sexual Enhancement (n = 68)

	# of Samples	% of Adulterated Samples
Total	68	100%
>1 Drugs Detected	41	60%
1 Drug Detected	27	40%
2 Drugs Detected	33	49%
3 Drugs Detected	6	9%
4 Drugs Detected	2	3%

LC/MS analyses (Table 1). In total, 60% (41/68) of the positive samples contained two or more adulterants. Seven different PDE5 inhibitors were identified in the positive samples (Figure 1). Sildenafil was the most common adulterant (74%; 50/68), followed by tadalafil (59%; 40/68), dimethylsildenafil (15%; 10/68), thiodimethyl sildenafil (13%; 9/68), hydroxythiohomosildenafil (7%; 5/68), thiosildenafil (6%; 4/68), and hydroxyhomosildenafil (1%; 1/68). Eighty-seven percent (59/68) of positive samples contained sildenafil and/or at least one of its analogs. Forty-six percent (31/68) of the adulterated samples contained both tadalafil and sildenafil.

Importantly, eighteen percent (18/102) of the tested samples had been associated with previous FDA warnings listed in their Tainted Products Marketed as Dietary Supplements Database at the time of sampling. These warnings include recalls and public notifications (Table 3).[4] Of these warning-associated samples, 72% (13/18) were found to contain PDE5 inhibitors, although this association was not significant (Yates chi-square test statistic = 0.076; p = 0.783). Of the 13 samples that contained at least one PDE5 inhibitor and were associated with an FDA warning, 46% (6/13) contained at least one of the same adulterants reported by the FDA.

Out of the 102 tested samples, only 3% (3/102) did not have some form of warning statement listed in English on the packaging and one of these tested positive for adulteration. Sixty-seven percent (68/102) warned about use with preexisting medical conditions (43 of which were found to be adulterated), 51% (52/102) warned about use when taking

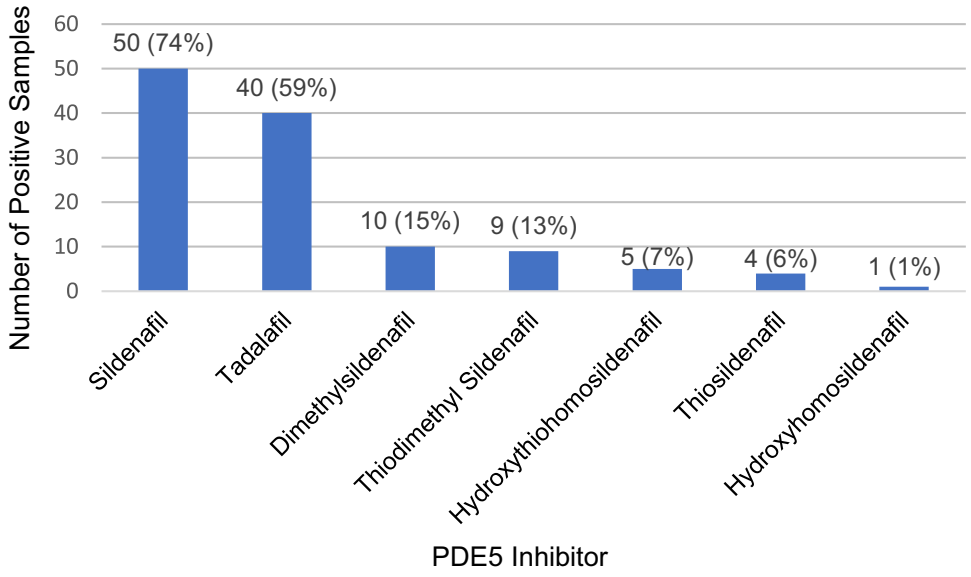

Figure 1 Number (and percent) of samples found to have each identified adulterant in the 2016 – 2017 survey of PDE5 inhibitor adulteration of products that were marketed as dietary supplements for sexual enhancement (n = 68).

Table 3 Adulterated Products Associated with a Previous FDA Warning in the 2016 – 2017 Survey of Products That Were Marketed as Dietary Supplements for Sexual Enhancement (n = 13)

Date(s) Product Was Purchased for FDLB Analysis[a]	Made in USA?	Adulterants Detected by FDLB	No. of Adulterants Detected by FDLB	No. of FDA Warnings	FDA Warning Type(s)	FDA Warning Adulterants	Date of FDA Warning(s)	At least one common Adulterant Detected by both FDA and FDLB?
9/12/2016 and 11/22/2016	Yes	Tadalafil	1	1	Public Notification	Sildenafil	3/5/2015	No
9/12/2016 and 11/22/2016	Yes	Hydroxythiohomosildenafil; Sildenafil; Tadalafil; Thiosildenafil	4	2	Recall; Public Notification	Sildenafil; Sulfoaildenafil; Thioaildenafil	12/17/12 and 2/28/2015	Yes
9/13/2016 and 11/22/2016	Yes	Sildenafil; Tadalafil	2	1	Public Notification	Sildenafil	4/30/2015	Yes
9/13/2016	Yes	Sildenafil; Tadalafil; Thiodimethyl sildenafil	3	2	Recall	Desmethyl carbondenafil; Dapoxetine	10/9/2015 and 10/28/2015	No
11/1/2016 and 11/22/2016	Yes	Dimethylsildenafil; Thiodimethyl sildenafil	2	1	Recall	Aminotadalafil; Sulfohydroxyhomosildenafil	3/12/2013	No
11/1/2016 and 6/27/2017	Yes	Hydroxyhomosildenafil; Hydroxythiohomosildenafil; Sildenafil; Thiosildenafil	4	1	Recall	Sildenafil; Sulfoaildenafil; Thioaildenafil	12/17/2012	Yes
11/1/2016 and 11/22/2016	Yes	Sildenafil; Tadalafil	2	1	Recall	Dapoxetine; Desmethylcarbondenafil	11/16/2013	No
11/22/2016 and 12/5/2016	Yes	Sildenafil; Tadalafil	2	1	Recall	Sildenafil; Tadalafil; Desmethyl carbodenafil	9/20/2017	Yes
4/13/2017	Unknown	Sildenafil	1	3	Public Notification; Recalls	Sildenafil; Sulfoaildenafil	3/3/15 and 8/10/10 and 11/5/09	Yes
4/13/2017	Yes	Sildenafil; Tadalafil; Thiosildenafil	3	1	Public Notification	Sildenafil	6/22/2017	No
5/30/2017	Yes	Sildenafil	1	1	Public Notification	Sildenafil	12/22/2016	Yes
6/27/2017	Yes	Sildenafil	1	1	Recall	Desmethyl carbondenafil; Dapoxetine	10/9/2015	No
9/8/2017	Yes	Tadalafil	1	1	Public Notification	Sildenafil	3/5/2015	No

Notes: [a]Some products were purchased from different locations on different dates if one location did not have enough product to constitute a sample for analysis. When this was necessary, products with the same lot # and expiration date were purchased.

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other medications (33 of which were found to be adulterated), 76% (78/102) warned about exceeding a maximum dose (65 of which were found to be adulterated), and 76% (78/102) warned against use by children (49 of which were found to be adulterated). All four of these warnings were included on the labels of 14% (14/102) of the samples (seven of which were found to be adulterated).

Seventy-eight percent (80/102) of the samples claimed that they were made in the US and 80% (64/80) of these were found to be adulterated. One of the samples claimed to be made in India, which was not found to be adulterated. The remaining 21 samples, four of which were found to be adulterated, did not state a country of origin on their packaging. Ninety-four percent (96/102) of the samples had a manufacturer or a distributor listed on the product label. Fifty-nine of these also included the city where the manufacturer or distributor is located. Fifty of the manufacturers/distributors were only associated with one sample, while the remaining 46 products had a manufacturer/distributor listed on the label of two or more different samples. One company was listed on the label of eight tested samples, all of which tested positive for adulteration, but did not have any indication of where the company was located.

Although none of the samples had PDE5 inhibitors listed among their ingredients, there were some commonly declared botanical ingredients across the sampled products. Forty-one percent (42/102) declared horny goat weed (*Epimedium* spp.), 40% (41/102) claimed to contain maca (*Lepidium meyenii*), and 25% (25/102) claimed to contain yohimbe (*Pausinystalia johimbe*), although declaration of these ingredients was not significantly associated with adulteration (Pearson's chi-squared test statistic, p value = 2.914, 0.088; 1.316, 0.251; and 2.207, 0.137, respectively). Seventy-two percent (73/102) of the samples tested were sold as single-pill blister packs and 89% (65/73) of these were found to be adulterated. Twenty-eight percent (29/102) of the samples were sold in a bottle, and 10% (3/29) of these were found to be adulterated. Samples purchased in blister packs were significantly more likely to be adulterated than samples purchased in bottles (Fisher's exact test, OR = 70.417; p-value <0.0001; 95% CI 15.175 – 382.4).

Discussion

Hidden drug ingredients were detected in 67% of products marketed as DS for sexual enhancement purchased from retail locations in the Sacramento area. Over half of these contained more than one drug ingredient and most were purchased from gas stations, liquor/cigarette stores, mini marts, or corner markets. The testing results confirm what the FDA has reported for online or imported products marketed as DS for sexual enhancement, that they have been found to contain PDE5 inhibitors, making these products unapproved drugs. Most of the samples tested by the FDA were purchased online or were identified during screening of imports at international mail facilities. Our study builds upon FDA's findings by showing that these tainted products are making their way onto the shelves at retail locations in the Sacramento area of CA. Similar to trends observed in the Tainted Products Marketed as Dietary Supplements Database, FDLB testing has specifically detected sildenafil, analogs of sildenafil, and tadalafil in the sampled products marketed as DS for sexual enhancement.

Importantly, of the samples purchased that were associated with an FDA warning, 72% contained at least one hidden drug ingredient. A study published in 2014 looked at recalled tainted products marketed as DS and found that a number of these products were still on the market at least six months after being recalled, with over 60% of those tested still containing a hidden drug ingredient.[17] FDB's findings also suggest that these products continue to be an issue despite FDA warnings. These results correlate with other studies that suggest that DS safety may not be ensured through the current regulatory system, which primarily relies on post-market surveillance and enforcement.[18–23] Interestingly, 54% percent of the adulterated samples that were associated with an FDA warning did not contain the same adulterants reported by the FDA. This indicates that these manufacturers have access to multiple active pharmaceutical ingredients that can be added to their products to make new formulations. Other publications also describe these issues and suggest recommendations, including congressional action to change the law and increase the FDA's enforcement powers and oversight.[18,20] Examples of such actions include reforming the Dietary Supplement Health and Education Act of 1994 and more effective enforcement tools that could allow agencies like FDA and FDB to immediately revoke a license if the product is found to be adulterated.[18,20] FDB is also using other approaches to address this issue, such as educating the public, including health care professionals, on the dangers of adulterated supplements. FDB recently published a survey study conducted to assess knowledge, attitudes, and practices surrounding dietary supplements among CA health care

professionals and assess factors contributing to the frequency with which health care professionals they discuss DS with patients; FDB is sharing data-driven educational materials in areas of knowledge limitations that were developed in response to this survey to help inform the health care professionals.[24]

Many of the tested samples, including a majority of those that were found to be adulterated, indicated that they were made in the US on the packaging. However, FDA sampling has frequently identified fraudulent DS entering the US through screening at international mail facilities.[4] Approximately 546,600 DS shipments entered the US from 2008 to 2011.[25] Additionally, 24% of tainted DS subject to a class I recall from 2004 to 2012 were manufactured outside of the US.[26] More recently, a review of FDA news releases regarding dietary supplement-related cases, introduced or decided in US federal courts between 2010 and 2019, found that more than half the cases involved defendants charged with introducing misbranded food or drugs into interstate commerce, including those contaminated with ED medications.[21] Counterfeit and imported supplements and illegal drugs continue to be a problem in the US as well as globally.[21,22,27–30] In 2020, the Natural Products Association urged the FDA to take action on imported adulterated dietary supplements.[23] It is possible that sexual enhancement products purchased in CA retail locations are manufactured in the US, as indicated on their packaging. It is also possible that these products are imported from other countries and are misbranded as made in the US. In recent years, the FDA's Office of Criminal Investigations has prosecuted multiple individuals for illegally distributing counterfeit Viagra, counterfeit Cialis, or tainted products marketed as sexual enhancement DS imported from China.[27,31–34] Some of these criminal investigations involved CA residents.[27,33,34]

Many products tested in this study, including those that were found to be tainted with pharmaceutical ingredients, claimed to contain botanical aphrodisiacs, commonly, but not limited to yohimbe, maca, horny goat weed, or a combination of these. For botanical/natural products with published human trials, including yohimbe and maca, one study suggested that evidence of their efficacy in treating ED is modest at best.[35] Pharmaceutical PDE5 inhibitors at certain defined doses on the other hand, have proven effectiveness for the treatment of ED. This provides reasonable motivation for adulterating DS marketed for sexual enhancement with these active pharmaceutical ingredients.

Tadalafil is the active ingredient in the prescription drug Cialis (manufactured by Eli Lilly for ED).[36] The package insert recommends a dose of 10 mg taken prior to sexual activity, but this dose can be adjusted to anywhere from 5 to 20 mg, once per day.[36] Sildenafil is the active ingredient in the prescription drug Viagra (manufactured by Pfizer, Inc. for ED).[37] The package insert for Viagra recommends a dose of 50 mg once per day, but this can range from 25 to 100 mg.[37] Forty-two percent (25/59) of the supplements that were adulterated with sildenafil and/or tadalafil contain levels of prescription drugs at or exceeding the minimum recommended prescription dosages (Figure 2). The safety of the doses of analogues is unknown.

None of the samples collected in this study declared pharmaceutical ingredients on their labels, and individuals purchasing these products potentially consume drug ingredients unknowingly. These ingredients are present at varying dosages and have not been characterized as safe and effective by the FDA. The fact that the products contain pharmaceutical drug dosages at prescription levels indicates that their presence in these dietary supplements is not accidental and may pose a significant public health concern. Additionally, over half of sexual enhancement products

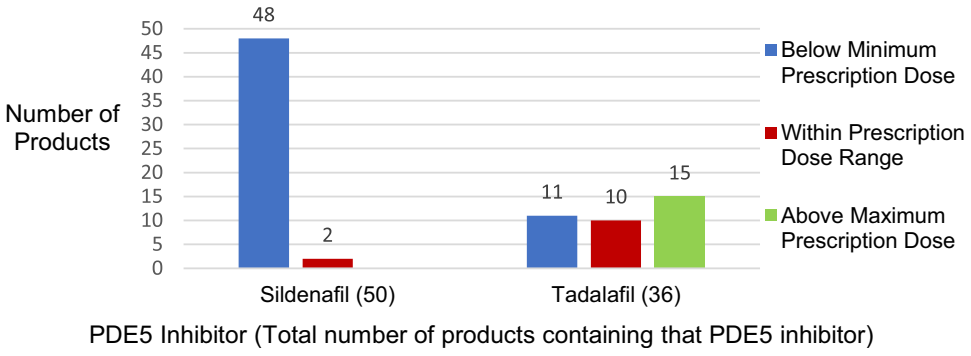

Figure 2 Number of products and estimated dose of detected PDE5 inhibitors with approved prescription dosage recommendations in the 2016 – 2017 survey of PDE5 inhibitor adulteration of products that were marketed as dietary supplements for sexual enhancement (n = 59). The prescription dose used for sildenafil is 25–100mg. The prescription dose used for tadalafil is 5–20mg.

identified as tainted in this study contained more than one active pharmaceutical ingredient. It is unknown how these PDE5 inhibitors react when combined together, but it is known that they can cause serious side effects when taken with prescription nitrates including decreasing blood pressure to dangerously low levels.[7] People suffering from heart disease and taking prescription nitrates would not be prescribed PDE5 inhibitors if experiencing ED and may be inclined to take a DS to manage their ED. Presence of multiple undeclared adulterants or active pharmaceutical ingredients in the sexual enhancement products increases the potential for severe adverse health consequences. Dietary supplements are generally considered and marketed to be "all natural" and therefore safe. It is possible that consumers use them without reservation, even with warnings on the packaging.

It is likely that adverse health events associated with these products disproportionately affect individuals who do not have or do not seek access to prescription medications for ED. Most positive samples in this study were sold as single-pill blister packs at gas stations or liquor stores/corner markets. Observations from sampling indicate that the products are commonly on display near the register; these products are easily accessible to a wide range of populations, including those who may be less informed and more vulnerable than those who intentionally seek out DS at health/nutrition stores or pharmacies or manage their ED with a prescribed medication.

This study had a few limitations. Sampling for this study was convenience-based; it was not randomized, and products purchased are not necessarily representative of all products marketed for sexual enhancement available to or utilized by the Sacramento population. Additionally, sampling for this study was performed in a specific area in north-central California and may not be representative of the rest of California or other states. The products were also purchased 6 to 7 years ago and adulteration frequency may have changed since this time. The study had a small sample size, and results of this study are limited to the 19 compounds for which the method is set up to screen. It is unknown what ingredients are present in these supplements beyond the PDE5 inhibitors listed in Table 1. Finally, although it was possible to obtain semi quantitative estimates using limited standard samples and matrix spikes with known concentrations in the same analytical batch, the laboratory method utilized for analysis is qualitative in nature.

Overall, in response to the FDA's findings, FDB initiated this study of products marketed for sexual enhancement and sold in retail locations across the Sacramento area to assess the presence of PDE5 inhibitor adulteration. Results from this study mirror FDA findings. First, our data confirm that adulterated products marketed as sexual enhancement DS commonly contain sildenafil and tadalafil. Second, more than one hidden drug ingredient was detected in many of the samples that were found to be adulterated in this study. As FDA sampling has focused on dietary supplements found online or through import screenings, our results add to FDA findings by demonstrating that tainted products are also sold at retail locations in California. Based on findings from this study, products marketed as supplements with sexual enhancement claims that are sold at health/nutrition stores or pharmacies, or in bottles, are less likely to contain PDE5 inhibitors than those available in single serving blister packs typically found at gas stations, cigarette/liquor stores, or corner markets.

Conclusion

This study identified PDE5 inhibitors in products marketed as sexual enhancement DS and sold in the greater Sacramento area of CA; these identified active pharmaceutical ingredients were present at varying dosages, which have not been characterized as safe and effective by the FDA. Some of the products tested were subject to prior FDA warnings and most of those were found to continue to have PDE5 inhibitor adulteration even after FDA action.

Many consumers continue to assume that DS are all natural and therefore safe. These adulterated supplements have the potential to cause severe adverse health effects due to accidental misuse, overuse, or interaction with other medications, or other drugs within the same product. They may also interfere with other underlying health conditions. It is therefore essential to raise awareness of this potentially significant public health concern.

Disclaimer

The findings and conclusions in this article are those of the authors and do not necessarily represent the views or opinions of the California Department of Public Health or the California Health and Human Services Agency.

Abbreviations

FDA, Food and Drug Administration; CDPH, California Department of Public Health; FDB, Food and Drug Branch; FDLB, Food and Drug Laboratory Branch; DS, dietary supplements; PDE5, Phosphodiesterase-5; ED, Erectile dysfunction; LC/MS, liquid chromatography-mass spectrometry; CI, confidence interval; OR, odds ratio.

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Disclosure

The authors report no conflicts of interest in this work.

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