



Adulteration of herbal sexual enhancers and slimmers: The wish for better sexual well-being and perfect body can be risky



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ABSTRACT

The popularity of herbal medicines and dietary supplements is increasing all over the world due to the many side-effects assigned to synthetic drugs. Herbal remedies should be considered as safe, with no side-effects, but unfortunately, even if they are labelled as natural, large numbers of adulterants, not only with toxic heavy metals but also with undeclared synthetic substances, have been detected up to date. In this review, the most frequent instances of adulteration of herbal medicines and dietary supplements acting as sexual enhancers and slimming products are thoroughly discussed. The great success of synthetic phosphodiesterase type-5 (PDE-5) inhibitory drugs like sildenafil, vardenafil and tadalafil, used for the treatment of erectile dysfunction has made them, as well as their unapproved analogues, popular as adulterants in herbal dietary supplements. The second group among blockbuster products are herbal preparations for slimming purpose, as obesity and gaining weight are major problems worldwide. Here, sibutramine hydrochloride monohydrate, an anti-obesity drug which inhibits serotonergic and noradrenergic reuptake, seems to be the most common adulterant. Together with large numbers of its analogues, thyroid hormones, anorexigens, diuretics, stimulants, and laxative agents are also detected in most of tested diet supplements.

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1. Introduction

In the recent years, the popularity of herbal medicines and dietary supplements is increasing all over the world, due to the many side-effects related to synthetic drugs; hence people are continuously looking for “all-natural” products. The herbal medicinal products and dietary supplements are one of the most rapidly growing sectors throughout the world with annual sales in excess of several billion euros. For instance, De Luca et al. (2012) calculated that the annual turnover of the most important commercially relevant phytopharmaceuticals is valued at over \$25 billion in the USA alone. In addition, World Health Organization (WHO) estimates, at least 80% of the population in the developing countries still relies exclusively on traditional medicine (e.g., in some countries almost exclusively botanicals) for their primary health care

needs (Georgiev, 2013).

Herbal remedies should be considered as safe, effective, with no side effects, however this huge market provokes intentional adulteration towards higher profit margin. According to a survey of the Food Drug Administration (FDA) in the USA, between 2007 and 2014, undeclared drugs were detected in 572 dietary supplements and the main product categories being sexual enhancement (238 entries), weight loss (228), and muscle building (90; Justa Neves and Caldas, 2015). Undeclared drugs/synthetic compounds in botanical products can be not only toxic but also often interact with other prescription medications and hence results in adverse effects, which could be even life-threatening. Therefore, it is not always easy for the consumers to discriminate high-quality products from low-quality ones. Different methods and platforms are developed/being continuously developed in order to determine the quality of the botanical products, ranging from classical macroscopic and microscopic techniques to modern DNA-barcoding authentication methods, as well as spectroscopic methods like vibrational (i.e., infrared, near-infrared and Raman spectroscopy among others) and nuclear magnetic resonance (NMR) spectroscopy and

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chromatographic and hyphenated methods such as high-performance liquid chromatography (HPLC) and ultra HPLC (UHPLC), gas chromatography and liquid chromatography in tandem with mass spectrometry (GC-MS and LC-MS, respectively) (Nunes, 2014; Pferschy-Wenzig and Bauer, 2015).

The present review focuses on the most frequent instances of adulteration of herbal medicines and dietary supplements, acting as sexual enhancers and slimming products and aims to stress out on the common problems and future challenges, related to the safety of herbal medicinal products, including contamination, intentional adulteration and product mislabeling, lack of standardization in some countries and the urgent necessity of the development of standardized criteria for herbal preparation. Besides that, public awareness should be tremendously increased on the potential risks of the use of unlicensed herbal medicines.

2. Sexual enhancers

2.1. Status of sexual enhancer, sold as drugs

Male erectile dysfunction (ED) affects ca. 150 million men worldwide and this number is expected to increase to about 300 million in 2025 (Schramek et al., 2014). Sildenafil citrate, vardenafil hydrochloride, and tadalafil (Fig. 1) are well-known phosphodiesterase-5 (PDE-5) inhibitors licensed for the treatment of erectile dysfunction, getting back millions of dollars incomes to the companies (Zou et al., 2006a). PDE-5 degrades the cyclic guanosine monophosphate (cGMP). As the molecular structures of the mentioned drugs are similar to that of cGMP, they maintain their higher levels, which relax smooth muscles, promote penile blood flow, and enhance erectile function (Reepmeyer and Woodruff, 2006; Singh et al., 2009). Despite the efficacy, numbers of serious drawbacks are described such as nausea, headache, facial flushing,

and dyspepsia, among others. What is more dangerous is that they interact with some other drugs such as widely used nitrates, what can cause a dramatic decrease of the blood pressure (Zou et al., 2006a).

As popularity of synthetic drugs used in treatment of erectile dysfunction was increasing tremendously, many herbal remedies and diet supplements were introduced as well. Several natural products for treatment of erectile-dysfunction have been known since ancient times. Among pure compounds alkaloids like **i**) yohimbine with α 2-adrenergic blocking activity, isolated for the first time from the bark of the West African tree *Pausinystalia johimbe* (K. Schum.) Pierre ex Beille. (Rubiaceae), **ii**) berberine widely distributed in Berberidaceae family, **iii**) combination of two vasodilators – papaverin and prostaglandin E₁ or pyrano-isoflavones, from the roots of *Eriosema kraussianum* N. E. Br. (Fabaceae) and diterpene forskolin from the Indian herb *Plectranthus barbatus* Andrews (Lamiaceae) - should be mentioned. Some chemical evidence supports the stimulatory action of the extract used in traditional medicines all over the world from *Tribulus terrestris* L. (devil's thorn, Zygophyllaceae), *Panax ginseng* (Araliaceae), *Lepidium meyenii* Walp. (maca, Solanaceae), *Eurycoma longifolia* Jack (Simaroubaceae) (Drewes et al., 2003), *Chlorophytum borivilianum* Santapau and Fernandes (Liliaceae) (Khanam et al., 2013), among others.

2.2. Risk of synthetic adulterations

Herbal remedies should be considered as safe with no side effects, but unfortunately, even if they are advertised as natural, large numbers of adulterants have been detected. In most cases, those are above mentioned three PDE-5 inhibitors, but also their analogues obtained after minor modifications of main molecular structures (Reepmeyer and Woodruff, 2006). Modification of

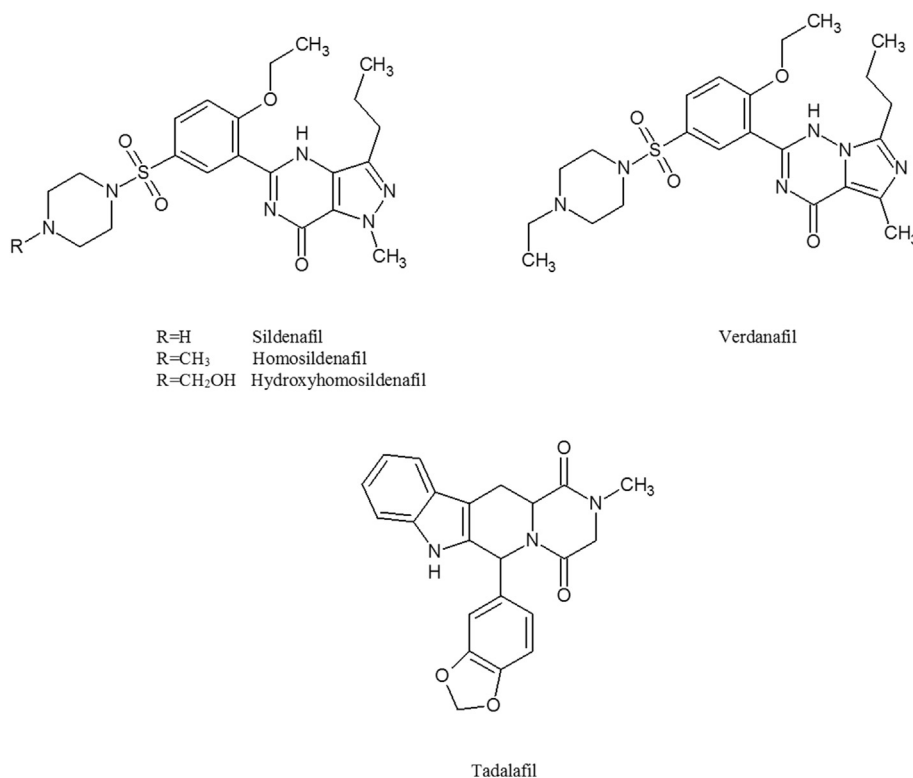


Fig. 1. Chemical structures of the most popular synthetic phosphodiesterase-5 inhibitors and its analogues.

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