

## Evaluation of Erectile Dysfunction Treatment Drugs Obtained Inappropriately in Japan

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### Abstract

The present study investigated the authenticity of sildenafil citrate that could be obtained through the internet without prescription in Japan. Loose Viagra<sup>®</sup> tablets were obtained from four 'personal import agents' operating Japanese internet websites. The four samples obtained were examined by infrared (IR) spectroscopic and high-performance liquid chromatographic (HPLC) analysis, and compared with authentic Viagra<sup>®</sup>. IR spectroscopic analysis showed all samples were confirmed to contain sildenafil citrate, which is the active pharmaceutical ingredient for Viagra<sup>®</sup>. However, the formulations seem to be different from that of authentic Viagra<sup>®</sup>, because of different IR spectra around 3300cm<sup>-1</sup>. HPLC analysis showed samples-1, -2, -3 and -4 contained 88%, 88%, 89% and 106% active ingredient of authentic 100mg tablet, respectively. The amount of Viagra<sup>®</sup> imported without prescriptions are estimated to increase sharply. A considerable number of these tablets seem to be counterfeit produced under poor hygienic conditions. In order to ensure that patients have safe and effective medicines, regulators, pharmaceutical companies, and physicians should enlighten patients to avoid purchasing them through the inappropriate routes.

Key words: sildenafil citrate, IR spectroscopic analysis, HPLC analysis

### Background

The prevalence of erectile dysfunction (ED) is estimated to be 20% in men in their age of 50s, and increases by age up to 64.4% in men in their 70s in Japan (1), and significant independent risk factors for ED have been known to be aging, hypertension, diabetes mellitus, heart disease, chronic hepatitis, disc herniation, cerebral infarction and other chronic diseases which may affect cardiovascular, neural or endocrine systems.

Oral administration of selective phosphodiesterase inhibitors have been shown to be effective and safe treatment modality of ED for the past 10 years, however, certain number of Japanese men feel embarrassed sharing details about ED, and feel uncomfortable to consult medical doctors about ED, although they are aware of the symptoms. Therefore, to maintain anonymity, many men obtain drugs through the internet, and it has been reported that hundreds of thousands of counterfeit ED treatment tablets were seized in Japan in 2006. Present study investigated the authenticity of sildenafil citrate which could be obtained without prescription in Japan.

## Materials and Methods

In October 2006, suspected counterfeit Viagra<sup>®</sup> tablets of 100 mg were obtained from four 'personal import agents' operating Japanese internet websites. Obtained four samples were analyzed for their appearance and ingredient of the tablets comparing with that of authentic Viagra<sup>®</sup> tablets of 100 mg.

Visual inspection was performed comparing appearance including shape, colour in addition to weight of the samples with that of authentic Viagra<sup>®</sup>.

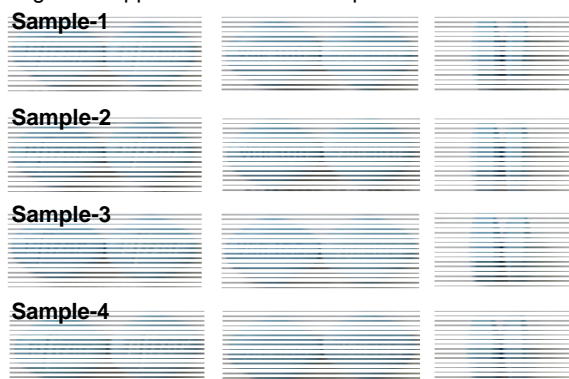
Chemical composition of the samples was tested utilizing near-infrared spectroscopy (NIRS). Principal components analysis was applied to the Viagra<sup>®</sup> tablet spectra to investigate similarity between four samples studied. Samples were measured as received. NIR spectra were recorded from both sides for at least three tablets of each sample, and wavelength correlation (WC) was used to compare NIR spectra.

Presence of sildenafil in four samples were examined by high-performance liquid chromatographic (HPLC) analysis by the courtesy of the manufacturer (Pfizer Ltd) and compared with authentic Viagra<sup>®</sup>.

## Results

Appearance and shape of each four samples were different from authentic Viagra<sup>®</sup> as shown in Figure 1. Weights of samples-1, -2, -3 and -4 were 663mg, 675mg, 677mg, and 667mg, respectively, and were heavier than authentic Viagra<sup>®</sup>, which weighed 620mg. From lateral viewing, all the samples were thicker than authentic one.

Figure 1. Appearances of the sample tablets

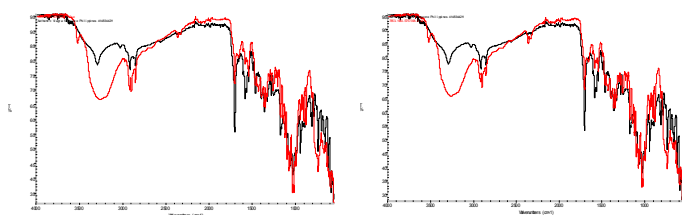


Sample-1, -2, -3 and -4 Tablets comparison images, in which authentic Viagra Tablets appear on the right.

IR spectroscopic analysis showed that samples-1, -2, -3 and -4 were confirmed to contain sildenafil citrate, which is active pharmaceutical ingredient for Viagra<sup>®</sup>, however, the formulations seems to be different from that of authentic Viagra<sup>®</sup>, because of different infrared spectra around 3300cm<sup>-1</sup> (Fig. 2, 3), although the formulations were not determined in the present study.

Figure 2. IR Spectroscopic analysis

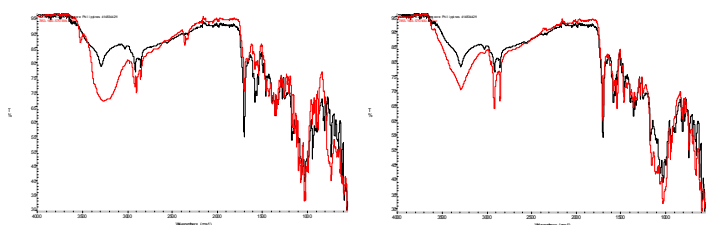
Sample-1      Sample-2



Overlays of Infrared Spectra from Subject Samples-1 and -2 (red) and from Authentic Viagra (black). The points of pattern concurrence demonstrate the presence of sildenafil citrate drug substance in the subject samples, while areas of pattern divergence show that the formulations of the samples are different from that of authentic Viagra.

Figure 3. IR Spectroscopic analysis

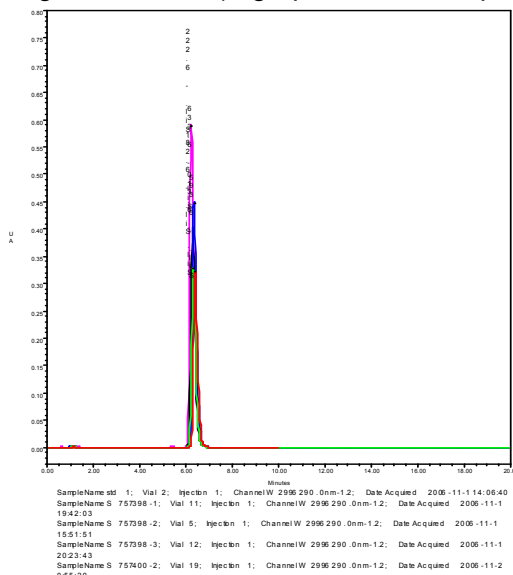
Sample-3      Sample-4



Overlays of Infrared Spectra from Subject Samples-3 and -4 (red) and from Authentic Viagra (black). The points of pattern concurrence demonstrate the presence of sildenafil citrate drug substance in the subject samples, while areas of pattern divergence show that the formulations of the samples are different from that of authentic Viagra.

HPLC analysis shows chromatographic overlays of Samples-1 (green), -2 (blue), -3 (black), -4 (pink), and Sildenafil Citrate Reference Material (red) (Fig. 4). The peak in the reference material at ~6.3-min corresponds to sildenafil, i.e. subject samples presented a peak at the retention time of ~6.3min for sildenafil, indicating the presence of sildenafil in the formulation of the four subject samples (Fig. 4),

Figure 4. HPLC (High-performance liquid chromatography)



Chromatographic overlays of samples-1 (green), -2 (blue), -3 (black), -4 (pink), and from sildenafil citrate reference material (red). The peak in the reference material at ~6.3-min corresponds to sildenafil. The subject samples presented a peak at the retention time of ~6.3min for sildenafil, indicating the presence of sildenafil in the formulation of the four subject samples.

The analysis showed samples-1, -2, -3 and -4 contained 88%, 88%, 89% and 106% active ingredient of authentic 100mg tablet, respectively.

## Discussion

Since the launch of Viagra<sup>®</sup> for ED, this medicament has been counterfeited. This is a threat to human health, because there is no quality management for the production and spreading of counterfeits. Viagra<sup>®</sup> counterfeits are made to look like Viagra, but in the current study, all the counterfeits could be discriminated by careful inspection. Viagra<sup>®</sup> counterfeits may or may not contain the active pharmacological ingredient of sildenafil citrate (2), however, IR spectroscopy showed that all the samples were almost similar but not identical to authentic Viagra<sup>®</sup> demonstrating the samples contained sildenafil citrate as well as from the results of HPLC analysis.

## Conclusions

With the spread of the internet, the amount of Viagra<sup>®</sup> imported without prescriptions are estimated to increase sharply. A considerable number of these tablets seem to be counterfeit produced under poor hygienic conditions. In order to ensure that patients have safe and effective medicines, regulators, pharmaceutical companies, and physicians should enlighten patients to avoid purchasing them through the inappropriate routes.

## References

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