

## Sildenafil Citrate for Women

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### Short Communication

Sildenafil citrate (SC) is a medicinal drug used to treat male erectile dysfunction and pulmonary hypertension. Sildenafil is a selective and potent competitive inhibitor of the cyclic guanosine monophosphate (cGMP) -specific phosphodiesterase-type 5 (PDE-5) enzymes, which, by preventing the breakdown of cGMP, potentiates the action of NO in tissues that contain PDE-5. Thus, increasing vasodilatation and potentiating the effects of nitrous oxide (NO) on the vascular smooth muscle [1-2]. SC increases uterine blood flow and potentiates estrogen-induced vasodilatation [3]. Sildenafil citrate is metabolized in the liver by cytochrome P450, the metabolites are: N-desmethylsildenafil (about 50% potency for PDE5). The biological half-life is from 3 to 4 hours, it is excreted in feces and in urine [4].

Sildenafil is developing as a potential applicant for the treatment of intrauterine growth retardation and for premature labor [5]. Sildenafil has also been proposed as a potential therapeutic strategy to maintain placental function in pre-eclampsia [6]. Should sildenafil citrate possess vasodilatory effects in the fetoplacental circulation, this would significantly enhance its therapeutic use in treating placental insufficiency. SC has recently been demonstrated not to alter the contractile response to vasoconstrictors or to endothelial dependent vasodilators. In non-pregnant females, SC

causes uterine artery vasodilatation therefore it also be employed to treat menstrual pain and muscle spasms [7]. SC is increasingly used in the pregnant patient for the treatment of pulmonary hypertension [8]. Its safety and efficacy combined with its lack of teratogenic or fetotoxic effects mean that its use for the treatment of pulmonary hypertension in pregnancy is likely to increase [9].

The most common adverse effects of sildenafil citrate use include: headache, flushing, indigestion, nasal congestion, and impaired vision, including photophobia and blurred vision. Some complained of blurriness and loss of peripheral vision. In July 2005, the FDA found that sildenafil could lead to vision impairment in rare cases [and several studies have linked sildenafil use with non-arteritic anterior ischemic optic neuropathy [10]. The FDA announced that all PDE5 inhibitors, including sildenafil, required a more prominent warning of the potential risk of sudden hearing loss [11]. Vaginal sildenafil might be an interesting therapeutic option before conception in women with histories of reproductive failure [12]. In addition, intravaginal sildenafil citrate tablets used as suppositories might be a new, interesting, safe antiabortive option in the treatment of threatened miscarriage in patients with a history of unexplained recurrent spontaneous abortion. The dose intravaginal sildenafil citrate is 25 tablets given 3- 4 times daily [13]. Oral dosage of SC is 50mg per day [14].

The International Index of Erectile Function (IIEF-5) Questionnaire					
Over the past 6 months:					
	Very low 1	Low 2	Moderate 3	High 4	Very high 5
1. How do you rate your confidence that you could get and keep an erection?					
2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/always 5
3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/always 5
4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	Extremely difficult 1	Very difficult 2	Difficult 3	Slightly difficult 4	Not difficult 5
5. When you attempted sexual intercourse, how often was it satisfactory for you?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/always 5

Figure 1: The international index of erectile function questionnaire [17].

In one study, vaginal application of sildenafil 25mg 4 times daily for 7 days plus estrogen (used to stimulate endometrial growth) resulted in successful conception in 3 of 4 patients in whom in vitro fertilization had failed due to inadequate endometrial development. [9] Less information is available for sexual dysfunction in women than on erectile dysfunction in men. The Index of Female Sexual Function (IFSF) is a 9-item questionnaire that was modeled after the international index of erectile function (IIEF) and tested for reliability and validity. The domains of the IFSF include quality of sexual intercourse, desire, orgasm, lubrication, clitoral stimulation, and overall satisfaction with sexual function [15]. There has been considerable interest in the effects of sildenafil in women, but the results have been somewhat disappointing. In a double-blind, placebo-controlled study of sildenafil in 583 women with female sexual arousal disorder, sildenafil 10, 50, and 100mg were no better than placebo in terms of effects on sexual function or frequency of intercourse [16,17] (Figure 1).

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