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Review Article

Brief Review on Sildenafil

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Abstract

The efficiency of sildenafil citrate, an oral agent for the treatment of erectile dysfunction, has been demonstrated in global studies, this randomised, double blind, placebo controlled, parlled, group, flexible dose study assessed the efficacy and safety of sildenafil to treat erectile dysfunction in men. Numerous articles have suggested that it improves endothelial function and a possible role in premature eujactulation or teatment of lower urinary tract symptoms. Drug approval and market development of sildenafil showed promise as an oral treatment for erectile dysfunction and it was lanced by pfizer as viagra. It is associated with rapid onset of action with in 14 minutes for some men and an extended duration of action for upto 12 hours.

Keywords: Phosphodiesterase Inhibitors; Safety; Side Effects; Viagra; Erectile Dysfunction

Introduction

Sildenafil citrate comes under class phosphodiesterase type 5 inhibitors its chemical name 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3d]pyrimidin-5-yl)-4-ethoxyphenyl] sulfonyl]-4-methyl piperazine citrate. Its Molecular Formula $C_{22}H_{30}N_6O_4S$. $C_6H_8O_7$, Its CAS Number 171599-83-0 And there other Brands are Revatio, Viagra. Vasodilating agents as a phosphodiesterase type 5 inhibitor [1]. Sildenafil is an oral drug for erectile dysfunction in the market. Drug approval and market development of sildenafil showed as an oral treatment for erectile dysfunction, it is launched by pfizer as brand name of viagra. Then three more phosphodiesterase type 5 inhibitor have been lanced in UK in 1989 sildenafil a drug that selectively target and powerfully inhibits the enzyme phosphodiesterase type 5 inhibitor, is the first synthesized and tested in pfizer's UK laboratory. the first trial of sildenafil is treated for coronary heart disease, it is ineffective but penile erection is noticed as a side effect. In 2002, tadalafil is approved for the treatment of erectile dysfunction by the europian medical agency in November, and by the US food and drug administration in november. In 2003, vardenafil is approved by the europian medical agency in March, and by the US food and drug administration in August. In 2007, the europian commision approved low dose of 2.5mg and 5.0mg tadalafil as single daily erectile dysfunction therapy. The pfizer withdraw an application to the europian medical agency to market viagra over the counter for erectile dysfunction that does not require any medical supervision, which could delay diagnosis of possible cardiovascular disease. In the year 2009, Boots has become the first United Kingdom pharmacy which offer Viagra without any need of a prescription. Tesco breaks into the Viagra market and offers the drug to customers without a prescription under a patient group direction. Vardenafil of 10mg is the first phosphodiesterase type 5 inhibitor introduced for erectile dysfunction in an orodispersible tablet. In 2012, Avanafil is approved for treatment of erectile dysfunction by the US Food and Drug Administration in April and by the europian medical agency in June 2013. The United Kingdom patent on Viagra expires opening the way for generic versions of sildenafil to be launched. In the year 2014, Manufacturer of Cialis, Lilly, agrees a deal with Sanofi to allow the French firm to buy exclusive rights to apply and to sell Cialis as a non-prescription medicine in Europe, the United States, and Australia after certain patents expire. In recent years the Medicines and Healthcare products Regulatory Agency recommends sildenafil 50mg should be available as a pharmacy medicine, and launches a consultation that closes in April [2]. Phosphodiesterase type 5 inhibitor inhibitors

increases blood flow to the penis during sexual stimulation. Phosphodiesterase type 5 inhibitor inhibitors are effective, there are differences in their onset and duration of action.

Erectile dysfunction is when a man has difficulty getting an erection. Keeping it long enough for sex. It's also known as erectile dysfunction or impotence. When not enough blood flows to the penis, preventing an erection. Some guys with erectile dysfunction find it difficult to either get or keep an erection every time they try to have sex [3]. Erectile dysfunction is often caused by something physical, such as disease, injury, or side effects from other drugs. In some men, erectile dysfunction is a side effect of some medication. These medications might include drugs used to treat; high blood pressure, heart disease, depression.

Figure 1

Mechanism of action

Figure 2

The physiologic mechanism of erection of the penis involves release of nitric oxide in the corpus cavernosum. Nitric oxide then activates the enzyme guanylate cyclase, which results in increased levels of cyclic guanosine monophosphate (cGMP), it produces smooth muscle relaxation in the corpus cavernosum and allowing inflow of blood. Sildenafil has no direct relaxant effect on isolated human corpus cavernosum, but enhances the effect of nitric oxide by inhibiting phosphodiesterase type 5, which is responsible for degradation of cGMP in the corpus cavernosum. They sexual stimulation causes local release of Nitric oxide, and inhibition of phosphodiesterase type 5 by sildenafil causes increased levels of cyclic guanosine monophosphate in the corpus cavernosum, resulting in smooth muscle relaxation and inflow of blood, In addition to human corpus cavernosum smooth muscle, phosphodiesterase type 5 is also found in lower concentrations in other tissues including platelets, vascular, visceral smooth muscle, and skeletal muscle. The inhibition of phosphodiesterase type 5 in these tissues by sildenafil which may be the basis for the enhanced platelet antiaggregant activity of nitric oxide observed *in vitro*, an inhibition of platelet thrombus formation *in vivo* and peripheral arterial-venous dilatation *in vivo.*

Pharmacokinetics and Metabolism of sildenafil is rapidly absorbed after oral administration, with a mean absolute bioavailability of 41%, Its pharmacokinetics of dose-proportional over the recommended dose range. It is eliminated predominantly by hepatic metabolism and it is converted to an active metabolite with properties similar to the parent sildenafil. The metabolite have half lives of 4 hours. Absorption and Distribution of sildenafil is rapidly absorbed. indicating distribution into the tissues. Sildenafil and its major circulating N-desmethyl metabolite approximately 95% bound to plasma proteins. Protein binding is independent of total drug concentrations, Based upon measurements of sildenafil in semen of healthy volunteers 90 minutes after dosing, less than 0.001% of the administered dose may appear in patients. Metabolism and Excretion of Sildenafil is cleared predominantly by the CYP3A4 by major route and CYP2C9 by minor route hepatic microsomal isoenzymes. This metabolite has a PDE selectivity profile similar to sildenafil and an *in vitro* potency for phosphodiesterase type 5 inhibitors approximately 50% of drug. After either oral or intravenous administration, sildenafil is excreted as metabolites predominantly in the feces that means approximately 80% of administered oral dose and to a lesser extent in the urine that means approximately 13% of the administered oral dose [4].

It is used to treat the male sexual problems. In combination with sexual stimulant, sildenafil works by increasing blood flow to the penis to help to get an erection and keep an erection. These drugs does not give protection against sexually transmitted diseases such as

- HIV
- Hepatitis B
- Gonorrach
- Syphilis.

Side effects

- Dizziness,
- Headache,
- Flushing, or stomach upset may occur.
- Vision changes such as increased sensitivity to light, blurred vision, or trouble telling blue and green colors apart may also occur [5].

Conclusion

Sildenafil is a treatment associated with a good safety and tolerability profile in men. Sildenafil significantly improves satisfaction and quality of life. From the basic and clinical research suggest possible roles in future for several other chronic conditions. Sildenafil is effective in several specific patient populations including the difficult to treat subpopulations such as diabetes mellitus ad after radical prostatectomy. It is associated with rapid onset of action with in 14 minutes for some men and an extended duration of action for upto 12 hours. It improves quality of life and satisfaction for men and it is well tolerated with a safety profile.

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