Published in final edited form as:
Exp Eye Res. 2011 July ; 93(1): 103–107. doi:10.1016/j.exer.2011.05.010.

Effect of Sildenafil Citrate on Intraocular Pressure and Blood Pressure in Human Volunteers

Rosana Gerometta[c], **Lawrence J. Alvarez**[a], and **Oscar A. Candia**[a,b]

[a] Department of Ophthalmology, Mount Sinai School of Medicine, Fifth Avenue and 100th Street, New York, NY 10029

[b] Department of Structural and Chemical Biology, Mount Sinai School of Medicine, Fifth Avenue and 100th Street, New York, NY 10029

[c] Departamento de Oftalmología, Facultad de Medicina, Universidad Nacional Del Nordeste (UNNE), Corrientes, Argentina

Abstract

Anecdotal reports have suggested that the vasodilator, sildenafil citrate, which evokes its effect via a select inhibition of PDE5, has the potential to increase intraocular pressure (IOP) in some individuals. An ocular hypertensive effect by sildenafil was also recently described in a sheep animal model. In contrast, clinical studies have not found a direct association between sildenafil ingestion (commonly consumed as Viagra) and changes in IOP. However, some such studies also reported no effects of sildenafil on systemic blood pressure (BP) at the time of the IOP determination. Given this surprising result, our purpose was to repeat a study in human volunteers in the city of Corrientes, Argentina to corroborate the effects of sildenafil on human IOP and systemic BP. For the present study, 9 healthy volunteers (male and female, 18 to 74 years old) were selected as subjects after ophthalmic and cardiovascular evaluation indicated that they exhibited normal parameters for their age. In a masked, placebo-controlled study, the subjects ingested 100 mg sildenafil citrate (provided as Vorst from Laboratorios Bernabo, Argentina) in one session, and a placebo on a second separate occasion. IOP was measured with a Goldman applanation tonometer by an ophthalmologist, and BP by a second physician, neither of whom witnessed the tablet ingestion by the volunteers, nor provided with information on the nature of the test compounds. A third individual administered the tablets. The average baseline IOP of this group of 9 was 13.1 ± 0.6 mm Hg. Subsequent to sildenafil ingestion, IOP increased by 26% to 16.5 ± 0.8 mm Hg 60 min later ($p < 0.005$, as paired data), and returned to control values within 2 hrs. Both systolic and diastolic BP were significantly reduced by sildenafil ingestion. At the point of maximal systemic hypotension (90 min), the systolic and diastolic pressures declined by 15% and 13%, respectively. No significant changes in IOP or BP were recorded after ingestion of the placebo. Our results suggest that sildenafil can elicit a transient IOP increase that may be of importance to patients chronically treated with PDE5 inhibitors for various vascular diseases (e.g., pulmonary hypertension). We discuss possible mechanisms by which PDE5 inhibition might lead to a rise in IOP.

Phone: (212) 241-6249; *Fax:* (212) 289-5945

Keywords

intraocular pressure; systolic pressure; diastolic pressure; Viagra; PDE5 inhibition; aqueous humor dynamics

1. Introduction

Sildenafil citrate (i.e., Viagra) is a potent cGMP-specific phosphodiesterase type 5 (PDE5) inhibitor (IC_{50} ≈4 nM) that is commonly administered to patients as an effective treatment for erectile dysfunction (Laties and Fraunfelder, 1999; Marmor and Kessler, 1999), as well as, for various vascular diseases, including pulmonary hypertension (Konstantinos and Petros, 2009). As a relatively potent systemic vasodilator, sildenafil was originally designed to treat cardiac ischemic conditions (Jackson et al., 1999; Konstantinos and Petros, 2009). Endothelium-derived relaxing factors (e.g., NO) diffuse into the smooth muscle and increase cGMP levels, which in turn produces muscle relaxation and dilation of blood vessels. The PDE5 inhibitors potentiate the muscle-relaxant effects of NO and cGMP (Laties and Fraunfelder, 1999; Marmor and Kessler, 1999).

Given the widespread application of this agent, and the fact that sildenafil is also relatively selective for PDE6 (IC_{50} ≈40 nM), which is solely found in the retina and is a critical enzyme in the regulation of the phototransduction cascade (Laties and Zrenner, 2002), several studies examined the effects of the PDE5 inhibitor on ocular blood flow and intraocular pressure (IOP) in both normal human subjects (Harris et al., 2008), and patients with age-related macular degeneration (Metelitsina et al., 2005). In general, no adverse effects of sildenafil on ocular circulation and IOP have been reported (Cordell et al., 2009; Grunwald et al., 2001b; Koksal et al., 2005; Harris et al., 2008; Yajima et al., 2000). However, the literature contained anecdotal reports observing an elevated IOP in senior patients (older than 70 years of age) who had taken sildenafil (Yajima et al., 2000). Because of the possibility that potent PDE5 inhibitors may increase IOP in a particular group of individuals, we recently tested the effects of sildenafil (and tadalafil, a longer lasting PDE5 inhibitor) on the IOP of a sheep animal model (Gerometta et al., 2010) Sheep were used because of the similarity to humans for their ocular response to topical glucocorticosteroid instillations and resulting ocular hypertension (Gerometta et al., 2009), which occurs due to a reduction in conventional outflow facility (Candia et al., 2010). Sheep also exhibited a robust increase in IOP one hour after oral ingestion of either sildenafil (50 and 100 mg) or tadalafil (20 mg). We earlier discussed in detail a potential model to explain the IOP rise secondary to sildenafil treatment (Gerometta et al., 2010).

Based on these observations, we found it remarkable that a study of the potential effects of sildenafil on the IOP of patients with primary open angle glaucoma (POAG) reported no effects of the drug on either IOP or systemic blood pressure (Grunwald et al., 2001a). Because this was an early report following the marketing of Viagra by Pfizer, we thought it important to re-examine these results, namely that sildenafil does not affect IOP or systemic blood pressure in human volunteers. For this, we recruited 9 healthy volunteers (3 female, 6 male) of various ages (18 to 74) who agreed to have their IOP and blood pressure simultaneously recorded in 2 sessions, one in which they received 100 mg sildenafil citrate, and the other in which they received a placebo. Our results indicate that sildenafil can potentially increase IOP in man, but the ocular hypertensive effect was transient and more variable among our human subjects than in sheep. However, the effect on human IOP coincided with the time course for which the drug is used clinically.

2. Materials and Methods

Volunteers were recruited via pamphlet announcements near and within the Universidad Nacional del Nordeste (UNNE) at Corrientes, Argentina, where the present study was conducted within the Cátedra de Oftalmología, Facultad de Medicina of UNNE. Nine healthy volunteers were selected as subjects after cardiovascular and ophthalmic evaluation showed normal parameters. The subjects were informed that they would be taking a pill and that they might feel weak for a period of 2 hours. They were told that they would be asked to return to the clinic for a second evaluation, at which time they would receive another pill. They were not told that in one session they would receive sildenafil, and in another session, a placebo. All subjects signed an informed-consent form approved by local agencies, which also follow the tenets of the Declaration of Helsinki. The subjects were recruited and tested in different sessions over a period of several months. IOP was measured with a Goldman applanation tonometer by an ophthalmologist and blood pressure (BP) by a second physician. Neither physician knew whether the subject had ingested sildenafil or the placebo. Sildenafil citrate was Vorst 100 mg (Laboratorios Bernabo, Argentina), which can be purchased at local pharmacies without prescription. Baseline IOP was measured at least twice before the administration of an agent. The right eye was measured first, and then the left eye of each patient, and then again over a period of between 60 to 165 min after ingestion of the administered tablet, which was provided by a third person not involved in the measurements. BP was measured immediately after the IOP determinations by the second physician, who was not in contact with the ophthalmologist or the individual administering the tablets.

Changes in measured IOP (mm Hg) and in systolic (Sys) and in diastolic (Dia) blood pressures (mm Hg) were analyzed using Student's t-test as paired values (before vs. after tablet ingestion) with $P < 0.05$ taken as the level of statistical significance.

3. Results

The 9 healthy volunteers recruited for this study ranged in age from 18 to 74 years old with an average age of 35.2 ± 16.9 (± SD) and a median age of 32. The subjects' ages are included along with their individual IOP and blood pressure values in the tables (1 through 4) described below.

The effects of sildenafil on IOP and systemic BP of the 9 volunteers are summarized in Tables 1 and 2. IOP before sildenafil was 13.1 ± 0.6, and increased to 16.5 ± 0.8 mm Hg ($P < 0.005$, as paired data) 60 min later (Table 1). IOP returned to control values within 2 hours, given that the IOP recorded at 2-hours post drug ingestion was 13.5 ± 0.5 mm Hg, a value indistinguishable from baseline ($P > 0.4$, as paired data). Not all of the volunteers were available for recording the IOP at 90-min post drug ingestion; but among those that were (the first 4 subjects listed in Table 1), there was an indication of an IOP decline in 3 of the 4 individuals by 90 min after drug ingestion. Table 1 also includes a compilation of the IOP measurements in all subjects that were taken 165 min after sildenafil was administered, at which point the average measured IOP was 12.8 ± 0.5 mm Hg, a value also indistinguishable from baseline ($P > 0.4$, as paired data).

At the point of maximal IOP elevation subsequent to sildenafil ingestion (60 min), the 3.4 ± 0.8 mm Hg pressure increase (Table 1) represented a 26% change over the control, baseline value.

In contrast to the markedly transitory effects on IOP, sildenafil administration elicited a prolonged systemic hypotensive effect on BP that persisted throughout the 165 min that the subjects were available for measurements (Table 2). The data indicate that the largest

systemic effect was on the systolic pressure at 60 and 90 min after the drug was ingested. Thereafter, there was a tendency for the systolic pressure to increase, but it remained significantly lower ($P < 0.05$, as paired data) than the control, baseline values when measured at 120 and 165 min post drug ingestion (Table 2). Diastolic pressure was also significantly reduced by sildenafil administration (Table 2).

At the point of maximal systemic hypotension (90 min), the systolic and diastolic pressures declined by 15% and 13%, respectively, relative to the baseline values.

When the same subjects ingested a placebo, there were no significant changes in their IOP and systemic blood pressure values (Tables 3 and 4).

4. Discussion

We obtained a 100% incidence of IOP elevation upon sildenafil ingestion among the volunteers in this study. In this regard, these results are in accord with our earlier observations with a sheep animal model, with which all animals administered sildenafil exhibited an increase in IOP (Gerometta et al., 2010). Moreover, our data are in apparent agreement with various anecdotal reports linking an increase in IOP to sildenafil treatment. Such anecdotes include reports of IOP elevation by patients and/or their physicians to the FDA following the marketing of the drug in 1998 (Laties and Fraunfelder, 1999, page 121), as well as, disparate reports from clinics in Europe that noted IOP elevations subsequent to sildenafil ingestion among some patients (Laties and Fraunfelder, 1999, page 120; Marmor and Kessler, 1999, page 160).

On the other hand, to the best of our knowledge, most if not all published reports of studies done on human volunteers have not demonstrated an association between sildenafil administration and elevations in IOP. Because of this, reviewers of this subject have considered IOP elevations among patients treated with sildenafil as coincidental and not treatment related (Laties and Zrenner, 2002; Laties, 2009).

At this time, we do not have a firm explanation for this discrepancy of results, but some plausible notions can be advanced. Human volunteers may not equally reach equivalent blood levels of the drug following oral ingestion due to differences in general health, metabolic efficiency, and/or individual dietary status at the time of the clinical test. After oral administration, dose-proportional maximum plasma concentrations of sildenafil are reached within 1 h (Nichols et al., 2002). Clinical effects have been noted within 12–30 min after dose administration to fasted patients (Eardley et al., 2002), but are delayed after a fatty meal (Nichols et al., 2002). The drug is rapidly eliminated from the body with a plasma half-life of 3–5 h (Boolell et al., 1996). Sildenafil is primarily metabolized by the low affinity cytochrome P450 enzyme 3A4 and secondarily by the high affinity enzyme 2C9 (Hyland et al., 2001). Overall, individuals older than 65 tend to have higher blood levels of the drug after ingestion due to lower metabolism; higher blood levels are also found in those with liver diseases and those with severe renal insufficiency (Pfizer product information for Viagra, published online January, 2010).

Some of these factors may have come into play within our group of volunteers given the variability of the differences in IOP between the baseline and post-sildenafil values among the individuals (Table 1). Our subjects varied in age, but all were tested in the early morning (beginning at 8:45 am) with few reporting that they had yet ingested breakfast, which in Corrientes commonly consists of a cup of coffee and toast. Importantly, the increase in IOP was recorded in tandem with a decrease in systemic pressure.

As aforementioned, we found it noteworthy that none of the POAG patients who volunteered to have their IOP measured following sildenafil ingestion exhibited a decline in BP concomitant with the time at which the IOP measurements were taken (Grunwald et al., 2001a). This suggested to us that the blood levels of the vasodilator may have been therapeutically low at the point of the IOP measurement. Nevertheless, there was a tendency in the Grunwald et al. (2001a) data for IOP to be somewhat elevated relative to placebo administration in their group of volunteers, but the difference was not statistically significant. We therefore suggest that had the IOP measurements been taken at the point of maximal blood levels (as presumably reflected by systemic hypotension), the IOP differences may have been larger.

In addition, we would like to note that we are aware of 5 other studies that measured the effects of sildenafil ingestion on IOP and/or ocular blood flow of human volunteers that also reported no changes in systemic blood pressure at the time the measurements were made (e.g., Dundar et al., 2006; Foresta et al., 2008; Grunwald et al., 2001b; Koksal et al., 2005; Polak et al., 2003). Overall, this suggests to us that the potential ocular hypertensive effects of sildenafil may have been overlooked.

Some ocular researchers seem to have expected *a priori* that sildenafil, as a systemic hypotensive agent, might evoke a reduction in IOP (and/or a direct reduction in blood flow to the optic nerve head) due to a decrease in ocular perfusion pressure. The latter is a theoretical concept that is in general defined as a difference between mean arterial pressure and IOP. Based on this theory, reductions in mean arterial pressure could potentially reduce blood flow into the eye and reduce IOP. However, sildenafil has been shown to increase ocular blood flow due to dilations of intraocular vasculature (Harris et al., 2008).

We previously discussed how sildenafil could potentially elicit an increase in IOP (Gerometta et al., 2010). One possibility is that the PDE5 inhibitor might have increased choroidal volume, given the fenestrated capillaries of the choroid, and the fact that the choroid is a vascular tissue analogous to the corpus cavernosum (Koksal et al., 2005; Marmor and Kessler, 1999; Paris et al., 2001). A putative increase in choroidal volume could have contributed to the IOP elevation (Kiel, 1994). It does indeed appear that sildenafil increases choroidal blood flow (Harris et al., 2008; Koksal et al., 2005). It also appears that sildenafil may increase the blood flow to the ciliary body via an increase in the flow of the posterior ciliary artery (Koksal et al., 2005). Such flow could result in a higher leak of plasma-like fluid from the fenestrated capillaries of the ciliary body, and subsequent leakage of such fluid directly into the anterior chamber across the front face of the iris, given the absence of an anatomical barrier at this surface (Bill, 1975; Freddo, 2001). Consistent with this possibility, we measured higher levels of protein in the anterior chamber of sheep following sildenafil ingestion (Gerometta et al., 2010).

It is also possible that ingestion of PDE5 inhibitors could increase the cGMP levels of anterior-segment ocular tissues involved in aqueous humor dynamics. There are reports that cGMP inhibits transport in the isolated porcine ciliary body (Fleischhauer et al., 2000; Shahidullah and Delamere, 2006), and that it increases aqueous outflow facility in a dose-dependent manner in monkeys (Kee, Kaufman and Gabelt, 1994). However, such reduction in fluid transport and increased outflow facility would have an effect on IOP opposite to the one that we observed. Thus, these possible effects seem to have been overwhelmed by the effect of sildenafil on ocular vascular flow, as judged by the increased protein content of the anterior chamber in the sheep animal model upon sildenafil ingestion (Gerometta et al., 2010). To whatever extent sildenafil increases cGMP levels in the ciliary epithelium and trabecular meshwork, thereby reducing IOP, such putative effect would serve to attenuate the magnitude of the IOP rise that we recorded.

From these observations we suggest that PDE5 inhibitors have the potential to increase IOP in patients, albeit transiently, and that this effect is presently not widely recognized. As such, individuals chronically treated with PDE5 inhibitors for various vascular diseases (e.g., pulmonary hypertension), especially senior patients, may unknowingly harm retinal ganglion cells secondary to IOP elevation, if they already have glaucoma, or are at risk for developing this disease. Transient, repetitive IOP elevations may lead to progressive vision loss in those with glaucoma (Werne et al., 2008). This consideration may be especially relevant to glaucoma patients taking tadalafil or other longer-lasting PDE5 inhibitors on a regular basis.

Our above suggestions are based on our results with sheep (Gerometta et al., 2010) and the present small study on human volunteers. In the latter group of healthy individuals, the mean IOP rise elicited by sildenafil of 3.4 mmHg, to a pressure of 16.5 mmHg (Table 1), may not appear salient within the context of pathological ocular hypertension. However, within our study group, three subjects had IOP increases of 5.5 and 8 mmHg, which in the latter case brought IOP to 21.5 mmHg. Thus, there is the potential that IOP could rise higher in individuals with reduced outflow facility, which is a common characteristic of POAG.

We would also like to point out that we measured 2 parameters (IOP and BP) and that while IOP went up, BP declined. On a single subject, with 2 parameters there are 4 possible outcomes - BP up with IOP up, BP up with IOP down, BP down with IOP up, and BP down with IOP down. To obtain one of these outcomes by chance in one subject, there is a probability of 0.25. With 2 subjects, the probability is 0.0625 that the 2 subjects exhibit the same outcome, e.g., BP down with IOP up, by chance. Dramatically, with 9 subjects, the probability that all would exhibit the same outcome by chance is 1/262,144. Thus, we conclude that the effect of sildenafil is highly significant for this very small population.

Our population included young people (an 18 and 20 year old) because sildenafil is easily obtained in Argentina without prescription and is regularly used by youths under the mistaken belief that the drug increases their sexual performance. In Argentina, there is much anecdotal evidence that the drug is frequently abused. Nevertheless, we suggest that a more extensive study on a larger and more diverse population should be completed to determine whether or not the observed ocular hypertensive effects of sildenafil are a particularity to these subjects in Corrientes. Such determination is important given the widespread use of this agent.

Acknowledgments

This work was supported by National Eye Institute Grants EY00160, EY01867 and EY13749, and by an unrestricted grant from Research to Prevent Blindness, Inc., New York, NY.

The authors thank Drs. Susana Frid, M.D. and Diocles Gomez-Chapo, M.D. for the measurements of IOP and blood pressure, respectively.

References

Bill A. Blood circulation and fluid dynamics in the eye. Physiol Rev. 1975; 55:383–417. [PubMed: 1153528]

Boolell M, Allen MJ, Ballard SA, Gepi-Attee S, Muirhead GJ, Naylor AM, Osterloh IH, Gingell C. Sildenafil: an orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile erectile dysfunction. Int J Impot Res. 1996; 8:47–52. [PubMed: 8858389]

Candia OA, Gerometta R, Millar JC, Podos SM. Suppression of corticosteroid-induced ocular hypertension in sheep by anecortave. Arch Ophthalmol. 2010; 128:338–343. [PubMed: 20212205]

Cordell WH, Maturi RK, Costigan TM, Marmor MF, Weleber RG, Coupland SG, Danis RP, McGettigan JW Jr, Antoszyk AN, Klise S, Sides GD. ERG Testing During Chronic PDE5 Inhibitor Administration (ERG-PDE5i) Consortium, 2009. Retinal effects of 6 months of daily use of tadalafil or sildenafil. Arch Ophthalmol. 127:367–373. [PubMed: 19365010]

Dundar SO, Dayanir Y, Topaloglu A, Dundar M, Kocak I. Effect of sildenafil on ocular hemodynamics in 3 months regular use. Int J Impot Res. 2006; 18:282–286. [PubMed: 16292333]

Eardley I, Ellis P, Boolell M, Wulff M. Onset and duration of action of sildenafil for the treatment of erectile dysfunction. Br J Clin Pharmacol. 2002; 53(Suppl 1):61S–65S. [PubMed: 11879261]

Fleischhauer JC, Beny JL, Flammer J, Haefliger IO. NO/cGMP pathway activation and membrane potential depolarization in pig ciliary epithelium. Invest Ophthalmol Vis Sci. 2000; 41:1759–1763. [PubMed: 10845596]

Foresta C, Caretta N, Zuccarello D, Poletti A, Biagioli A, Caretti L, Galan A. Expression of the PDE5 enzyme on human retinal tissue: new aspects of PDE5 inhibitors ocular side effects. Eye (Lond). 2008; 22:144–149. [PubMed: 17585311]

Freddo TF. Shifting the paradigm of the blood-aqueous barrier. Exp Eye Res. 2001; 73:581–592. [PubMed: 11747359]

Gerometta R, Alvarez LJ, Candia OA. Effects of sildenafil and tadalafil on intraocular pressure in sheep: implications for aqueous humor dynamics. Invest Ophthalmol Vis Sci. 2010; 51:3139–3144. [PubMed: 20089876]

Gerometta R, Podos SM, Danias J, Candia OA. Steroid-induced ocular hypertension in normal sheep. Invest Ophthalmol Vis Sci. 2009; 50:669–673. [PubMed: 18824726]

Grunwald JE, Jacob SS, Siu K, Piltz J, Dupont J. Acute effects of sldenafil ctrate (Viagra) on intraocular pressure in open-angle glaucoma. Am J Ophthalmol. 2001a; 132:872–874. [PubMed: 11730651]

Grunwald JE, Siu KK, Jacob SS, Dupont J. Effect of sildenafil citrate (Viagra) on the ocular circulation. Am J Ophthalmol. 2001b; 131:751–755. [PubMed: 11384572]

Harris A, Kagemann L, Ehrlich R, Ehrlich Y, Lopez CR, Purvin VA. The effect of sildenafil on ocular blood flow. Br J Ophthalmol. 2008; 92:469–473. [PubMed: 18369062]

Hyland R, Roe EG, Jones BC, Smith DA. Identification of the cytochrome P450 enzymes involved in the N-demethylation of sildenafil. Br J Clin Pharmacol. 2001; 51:239–248. [PubMed: 11298070]

Jackson G, Benjamin N, Jackson N, Allen MJ. Effects of sildenafil citrate on human hemodynamics. Am J Cardiol. 1999; 83:13C–20C.

Kee C, Kaufman PL, Gabelt BT. Effect of 8-Br cGMP on aqueous humor dynamics in monkeys. Invest Ophthalmol Vis Sci. 1994; 35:2769–2773. [PubMed: 8188471]

Kiel JW. Choroidal myogenic autoregulation and intraocular pressure. Exp Eye Res. 1994; 58:529–543. [PubMed: 7925690]

Koksal M, Ozdemir H, Kargi S, Yesilli C, Tomac S, Mahmutyazicioglu K, Mungan A. The effects of sildenafil on ocular blood flow. Acta Ophthalmol Scand. 2005; 83:355–359. [PubMed: 15948790]

Konstantinos G, Petros P. Phosphodiesterase-5 inhibitors: future perspectives. Curr Pharm Des. 2009; 15:3540–3551. [PubMed: 19860699]

Laties A, Zrenner E. Viagra (sildenafil citrate) and ophthalmology. Prog Retin Eye Res. 2002; 21:485–506. [PubMed: 12207947]

Laties AM. Vision disorders and phosphodiesterase type 5 inhibitors: a review of the evidence to date. Drug Saf. 2009; 32:1–18. [PubMed: 19132801]

Laties AM, Fraunfelder FT. Ocular safety of Viagra, (sildenafil citrate). Trans Am Ophthalmol Soc. 1999; 97:115–25. discussion 125–8. [PubMed: 10703120]

Marmor MF, Kessler R. Sildenafil (Viagra) and ophthalmology. Surv Ophthalmol. 1999; 44:153–162. [PubMed: 10541153]

Metelitsina TI, Grunwald JE, DuPont JC, Ying GS. Effect of Viagra on the foveolar choroidal circulation of AMD patients. Exp Eye Res. 2005; 81:159–164. [PubMed: 16080909]

Nichols DJ, Muirhead GJ, Harness JA. Pharmacokinetics of sildenafil after single oral doses in healthy male subjects: absolute bioavailability, food effects and dose proportionality. Br J Clin Pharmacol. 2002; 53(Suppl 1):5S–12S. [PubMed: 11879254]

Paris G, Sponsel WE, Sandoval SS, Elliott WR, Trigo Y, Sanford DK, Harison JM. Sildenafil increases ocular perfusion. Int Ophthalmol. 2001; 23:355–358. [PubMed: 11944862]

Polak K, Wimpissinger B, Berisha F, Georgopoulos M, Schmetterer L. Effects of sildenafil on retinal blood flow and flicker-induced retinal vasodilatation in healthy subjects. Invest Ophthalmol Vis Sci. 2003; 44:4872–4876. [PubMed: 14578411]

Shahidullah M, Delamere NA. NO donors inhibit Na, K-ATPase activity by a protein kinase G-dependent mechanism in the nonpigmented ciliary epithelium of the porcine eye. Br J Pharmacol. 2006; 148:871–880. [PubMed: 16770322]

Werne A, Harris A, Moore D, BenZion I, Siesky B. The circadian variations in systemic blood pressure, ocular perfusion pressure, and ocular blood flow: risk factors for glaucoma? Surv Ophthalmol. 2008; 53:559–567. [PubMed: 19026319]

Yajima T, Yajima Y, Koppiker N, Grunwald JE, Laties AM. No clinically important effects on intraocular pressure after short-term administration of sildenafil citrate (Viagra). Am J Ophthalmol. 2000; 129:675–676. [PubMed: 10844068]

Table 1

Effect of Sildenafil on IOP (mm Hg) of Human Volunteers

		Baseline Pressure				Pressure after Oral Sildenafil (100 mg) Administered at 9:15 am								Change in IOP from Baseline	
		8:45 am		9:15 am		10:15 am		10:45 am		11:15 am		12:00 pm		At 60 min	At 165 min
Subject Age	Sex	OD	OS	OD	OS	OD	OS	OD	OS	OD	OS	OD	OS		
30	F	13	13.5	14	13	14	14	10.5	12	11	12	11.5	12	0.5	−1.8
24	F	16	16	16	16	17.5	16	15	14	15	15	15	14	0.8	−1.5
74	M	10	12	10	10	15	16	15	15	13	12	11	10	5.5	0.5
44	F	15	15	16	15	18	18	16	17	16	16	15	15	2.5	−0.5
32	M	13	14	14	13	21	22			14	14	15	13	8.0	0.5
35	M	11	12	12	12	18	17			15	14.5	13	13	5.5	1.0
18	M	13	12	13	13	15	16			12.5	12	12	12	2.5	−1.0
40	M	12	12	11	12	15	16			13	13.5	12	13	4.0	1.0
20	M	12	12	12	13	14	14			12	12	12	11	1.5	−1.0
Mean:				13.1		16.5*				13.5		12.8		3.4	−0.3
SEM:				0.6		0.8				0.5		0.5		0.8	0.4
n:				9		9				9		9			

*Significantly greater than the 9:15 am baseline value (P< 0.005) as paired, two-tailed data.
Mean IOP was calculated from the average of the OD and OS values of each individual.

Table 2

Effect of Sildenafil on Systolic (Sys) and Diastolic (Dia) Blood Pressure (P; mm Hg) of Human Volunteers

		Baseline Pressure				Pressure after Oral Sildenafil (100 mg) Administered at 9:15 am								Change in Systolic Pressure from Baseline	
		8:45 am		9:15 am		10:15 am		10:45 am		11:15 am		12:00 pm		At 60 min	At 90 min
Subject Age	Sex	Sys P	Dia P	Sys P	Dia P	Sys P	Dia P	Sys P	Dia P	Sys P	Dia P	Sys P	Dia P		
30	F	110	70	110	70	90	50	85	50	110	70	100	60	−20	−25
24	F	100	70	100	60	95	60	90	60	90	60	90	60	−5	−10
74	M	135	90	140	80	110	70	100	60	120	75	130	80	−30	−40
44	F	110	70	110	70	110	60	85	55	110	70	100	60	0	−25
32	M	125	80	120	80	100	70	120	80	120	80	120	80	−20	0
35	M	130	80	130	90	110	80	110	80	120	80	130	80	−20	−20
18	M	110	75	110	70	100	70	90	60	100	70	110	70	−10	−20
40	M	130	80	130	80	125	80	120	80	125	80	120	80	−5	−10
20	M	115	75	110	75	100	60	100	60	100	60	95	60	−10	−10
Mean:				117.8	75.0	104.4*	66.7*	100.0*	65.0*	110.5*	71.7**	110.6*	70.0*	−13.4	−17.8
SEM:				4.3	2.9	3.5	3.3	4.6	3.9	3.9	2.6	5.0	3.3	3.2	3.9
n:				9	9	9	9	9	9	9	9	9	9	9	9

* Significantly less than its respective 9:15 am baseline value ($P < 0.05$) as paired, one-tailed data.

** Marginally less than its respective 9:15 am baseline value ($P < 0.06$) as paired, one-tailed data.

Exp Eye Res. Author manuscript; available in PMC 2012 July 1.

Table 3

Effect of Placebo on IOP (mm Hg) of Human Volunteers

		Baseline Pressure				Pressure after Oral Placebo Administered at 9:15 am								Change in IOP from Baseline	
		8:45 am		9:15 am		10:15 am		10:45 am		11:15 am		12:00 pm		At 60 min	At 165 min
Subject Age	Sex	OD	OS	OD	OS	OD	OS	OD	OS	OD	OS	OD	OS		
30	F	13	13.5	12.5	14	13	14	12	13	12.5	12	12	13	0.3	−0.8
24	F	16	16	15	16	15.5	16	15	16	15	14	16	15	0.3	0
74	M	10	11	10.5	10	11	10.5	10	11	11	10	11.5	10	0.5	0.5
44	F	16	15	16	15.5	15	15.5	15	16	15	15	16	15.5	−0.5	0
32	M	11	12	13	12	12	13			14	13	14	12.5	0	0.8
35	M	11	11	11.5	12.5	12	12			13	12	12.5	12	0	0.3
18	M	13	12	12	12	13	13			10	12	11	12.5	1	−0.3
40	M	13	13	12	13	13	13			12	13	13	13	0.5	0.5
20	M	12	12	12.5	13	14	14			12	11	12	12.5	1.5	−0.5
Mean:				12.9		13.3						13.0		0.4	0.1
SEM:				0.6		0.5						0.6		0.2	0.2
n:				9		9						9		9	9

Mean IOP was calculated from the average of the OD and OS values of each individual.

Table 4

Effect of Placebo on Systolic (Sys) and Diastolic (Dia) Blood Pressure (P; mm Hg) of Human Volunteers

		Baseline Pressure				Pressure after Oral Placebo Administered at 9:15 am								Change in Systolic Pressure from Baseline	
		8:45 am		9:15 am		10:15 am		10:45 am		11:15 am		12:00 pm		At 60 min	At 90 min
Subject Age	Sex	Sys P	Dia P	Sys P	Dia P	Sys P	Dia P	Sys P	Dia P	Sys P	Dia P	Sys P	Dia P		
30	F	110	65	110	70	110	70	110	70	110	70	110	70	0	0
24	F	100	65	100	70	100	70	100	70	100	65	100	70	0	0
74	M	135	85	140	80	135	75	135	80	140	85	135	80	−0.5	−0.5
44	F	110	70	110	75	110	65	110	70	110	75	110	75	0	0
32	M	125	80	120	80	125	80	120	80	125	80	125	80	5	0
35	M	130	80	130	85	130	80	135	80	130	80	135	85	0	5
18	M	110	70	100	70	100	70	110	70	110	70	110	70	0	10
40	M	130	85	130	80	120	80	130	80	125	80	130	85	−10	0
20	M	110	70	110	70	110	75	110	70	110	75	110	70	0	0
Mean:				116.7	75.6	115.6	73.9	117.8	74.4	117.8	75.6	118.3	76.1	−1.1	1.1
SEM:				4.7	2.0	4.2	1.8	4.3	1.8	4.3	2.1	4.3	2.2	1.4	1.4
n:				9	9	9	9	9	9	9	9	9	9	9	9