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The UNSIN Report
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SECTION I: AT A GLANCE (ABSTRACT)

**Sin explored:** Lust
**Specific molecular target:** Protein tyrosine phosphatase 1B

**Proposed intervention:**
An allosteric regulator, Nosexin, has been designed to intracellularly inhibit the activity of protein tyrosine phosphatase 1B (PTP1B) in dopaminergic pathways of the medial preoptic area (MPOA), mesolimbocortical (MLC) and nigrostriatal (NS) regions.

Prolactin (PRL) inhibits dopaminergic activity to attenuate lustful behaviour. Initially, PRL exerts a stimulatory effect on the synthesis of tyrosine hydroxylase (TH), a rate-limiting enzyme in dopamine (DA) synthesis. The effect exerted by PRL is amplified by the JAK2-STAT5b signalling cascade, with STAT5b being highly prevalent in the MPOA. PTP1B dephosphorylates STAT5b, thereby terminating the signalling cascade. Nosexin inhibits PTP1B, thus prolonging the stimulatory signal of PRL on DA production, with pronounced effects in the MPOA. After sustained stimulation of DA receptors, receptor desensitization occurs and results in dopaminergic inactivity.

Nosexin is administered intranasally using a spray, allowing the drug to bypass the blood-brain barrier and access the central nervous system (CNS). Its small size and high lipophilicity allows it to permeate cell membranes of dopaminergic cells. Modelled after known PTP1B inhibitors, Nosexin binds to Cys121, an allosteric site on PTP1B, to inhibit the enzyme’s catalytic function and prolong the activation of STAT5b.

The target population, sex offenders, will be required to take regular doses of Nosexin as part of their chronic treatment plan. The drug is administered before sleeping in order to exert maximal effects, as endogenous PRL levels are highest during non-rapid eye movement sleep.
SECTION II: FRAMING THE PROBLEM

Lust - A Definition
Lust, or elevated libido, is a conscious, overwhelming desire for sexual gratification, without the presence of emotional attachment. It can be dissected into two behavioural components: appetitive (motivation to pursue a sexual interest) and consummatory (engaging in sexual acts). Lust involves a complex interplay between various hormones and neurotransmitters acting in response to input from olfactory, tactile, visual and auditory stimuli. While levels of these signal molecules are mediated by the activity of the hypothalamic-pituitary-adrenal axis, it is the specific response to these molecules by the dopaminergic pathways of the brain that primarily regulates libido.

Biological Regulation of Lust
The hypothalamus plays a crucial role in the synthesis and pulsatile secretion of gonadotropin releasing hormone (GnRH), which stimulates the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the anterior pituitary. These hormones increase the gonadal production of estrogens and androgens that are vital in sustaining physiological reproductive functions. Further, following the input of attractive stimuli, hyperactivity in the medial preoptic area (MPOA), mesolimbocortical (MLC) and nigrostriatal (NS) dopaminergic pathways is primarily responsible for the expression of lustful behaviour and sexual arousal.

Potential Pathways for Intervention

Androgens
Elevated levels of testosterone and its potent metabolite, dihydroxytestosterone, are linked to increases in sexual desire. Both hormones act on androgen receptors (AR) to facilitate erectile function. Studies performed using AR antagonists show that a serum testosterone decrease of 30% directly decreases libido in hypergonadal men. However, evidence suggests that in healthy adult males and pre-menopausal women, circulating levels of serum testosterone are not consistent indicators for sex drive. In addition, testosterone is a precursor for estradiols, which are involved in a plethora of metabolic processes in the body. Thus, lowering testosterone levels may cause undesirable symptoms associated with deficient estrogen levels, such as an increased risk of vertebral fractures and atherosclerosis.

Oxytocin (OT)
The hypothalamus synthesizes oxytocin, a peptide hormone released into the bloodstream of both sexes. In rats, mice and rabbits, an increase in OT has been correlated with increased sexual stamina. As such, OT antagonists have been shown to be extremely effective in impairing copulation in rats. Similarly, in humans, elevated
plasma OT plays a large role in enhancing physical arousal, such as genital function and orgasm. Physical arousal may be a byproduct of lust; however, they are not synonymous. Thus, OT was not targeted due to the lack of evidence supporting its ability to stimulate the appetitive component of lust, specifically in the MPOA. Further, decreasing OT levels is not viable, for this can introduce adverse side-effects on crucial reproductive processes, such as follicular growth and lactation. Interfering with OT levels can also cause irregularities in psychological behaviours, such as parental care and attachment.

**Serotonin (5-HT)**
Serotonin has been found to exert both excitatory and inhibitory effects on sexual function, depending on the receptor subtype that it stimulates. Generally, however, high levels of 5-HT are associated with a lowered sex drive. When selective serotonin reuptake inhibitors are given to subjects for the purpose of treating depression, an increase in synaptic concentrations of 5-HT causes a decrease in libido. However, elevated 5-HT levels can result in ataxia, hallucinations, nausea, and tachycardia. Another significant adverse effect includes long-term, persistent dysfunction of sexual organs; however, inducing infertility is not the intention of our intervention. Thus, the risks of serotonin toxicity outweigh the potential benefits of decreased libido.

**Dopamine (DA)**
Dopamine is predominantly linked to the appetitive component of sexual behaviour. Increased dopaminergic activity in the brain’s motivation-reward centers, which include the MPOA, MLC and NS, have been implicated in the reinforcement of sex drive and appetite. 
D2 receptor antagonists in antipsychotic drugs mitigate libido and facilitate emotional repulsion from the opposite sex. However, because DA receptors are widespread throughout the CNS, as well as cardiovascular and renal systems, it is difficult to design a drug with high specificity so as to avoid unwanted side effects. Moreover, evidence suggests that D1 and D2 antagonists interfere with sleep cycles by altering the amount of time spent in REM sleep. In addition, low DA levels in the MLC and NS are linked to depression, Alzheimer’s and Parkinson’s disease; thus, this is not an ideal molecule to target directly.

**Prolactin (PRL)**
Prolactin is a circulating peptide hormone, primarily synthesized and released by lactotrophic cells in the anterior pituitary gland. Elevated PRL levels are strongly linked to reductions in both the appetitive and consummatory components of lust. Prolactin levels naturally spike in the body after orgasm during the sexual refractory period to partially contribute to sexual satiation. Men with elevated PRL serum levels (>200µg/L) due to prolactinoma suffer from deficient GnRH and testosterone levels, and report noticeable libido impairment. Furthermore, in a study of hyperprolactinemic subjects, 58.5% reported increased libido after 24-months of treatment aimed to normalize PRL levels. Another study conducted on over 300 hyperprolactinemic men showed that 88% of subjects experienced erectile dysfunction, a symptom linked with decreased libido. Treatment with bromocriptine, a DA agonist, decreased serum PRL levels and restored libido.
In order to exert inhibitory effects on lust, PRL, once secreted into the bloodstream, enters the CNS through cerebrospinal fluid. Upon binding to a cytokine prolactin receptor (PRLR) on the plasma membrane of target cells in the MPOA, MLC and NS, PRL causes two receptors to dimerize. A signal transduction mechanism consisting of the JAK2-STAT5b pathway is then initiated, beginning with the activation of JAK2 proteins, which subsequently phosphorylate STAT5b proteins. Within 5 minutes, cytoplasmic STAT5b dimers begin to translocate into the nucleus to activate the transcription of tyrosine hydroxylase (TH), a rate-limiting enzyme that catalyzes DA production. Sustained DA synthesis and release causes desensitization of DA receptors in the MPOA, MLC and NS, thus inhibiting dopaminergic activity to attenuate lust.

To exaggerate the effects of PRL, one may add exogenous PRL or a similar agonist. However, this would procure less effective results. PRLRs are widely distributed throughout the body and interfering with them may elicit unwanted side effects in a multitude of essential processes, such as reproduction, lactation and amenorrhea. Even if PRLR selectivity was achieved, rat studies show that inducing acute hyperprolactinemia facilitates sexual activity, while chronic hyperprolactinemia consistently inhibits libido. This is because after PRL treatment, TH activity and DA release peaks for 1-4 hours before DA receptor desensitization occurs. Further, in normal rats, low doses of subcutaneous PRL-injections that raise serum-PRL levels to 50 µg/L (within normal physiological range) were found to increase the frequency of mounts and ejaculation by approximately 38% and 110%, respectively. These results suggest that alternate factors, such as oxytocin and opioids, may better account for the sense of gratification experienced after orgasm. Thus, introducing low, acute doses of PRL to mimic the sexual refractory period was not selected as a method of intervention.

Moreover, chronic administration of exogenous PRL is shown to stimulate the endocytosis, ubiquitination and degradation of PRLRs in an effort to down-regulate the PRL response. Due to this, exogenous PRL will ultimately be ineffective at attenuating lust. Rather, inhibiting termination enzymes, such as PTP1B, of the signalling cascade would be more effective, as STAT5b proteins will remain active for an extended period of time regardless of whether PRL is acting on PRLRs.

Ultimately, PRL is the best locus for intervention, as it is most closely linked to the regulation of dopaminergic activity in the MPOA, MLC and NS, which are areas of the brain that have been identified as primary regulators of libido and sexual desire. As demonstrated thus far, manipulating the effects of endogenous PRL through the inhibition of signal termination mechanisms appears to be most effective in mitigating libido. If the correct approach is taken, adverse effects can be minimized.
SECTION III: ACCOMPLISHMENTS, FUTURE PLANS & JYP

Introduction

Lust, defined as elevated libido, is an overwhelming desire for sexual gratification, and is characterized by appetitive and consummatory behaviours. The motivation and action of pursuing a sexual interest is regulated by three dopaminergic regions: the medial preoptic area (MPOA), mesolimbocortical (MLC) and nigrostriatal (NS) pathways.\textsuperscript{17,20,31,35,38,40} Prolactin, a peptide hormone produced by lactotrophs in the anterior pituitary, is an effective inhibitor of dopaminergic activity in these regions\textsuperscript{31}, and thus functions to attenuate lust.\textsuperscript{25,38} This inhibitory effect is exerted by the activation of the JAK2-STAT5b signalling cascade, which stimulates the transcription and synthesis of tyrosine hydroxylase (TH).\textsuperscript{9,12} This enzyme catalyzes dopamine (DA) production, consequently producing excess amounts of DA for approximately 1 to 4 hours.\textsuperscript{33} Extended stimulation desensitizes DA receptors\textsuperscript{9,18,33}, thus reducing dopaminergic activity and inhibiting lust.

Intervention

The prolactin-induced JAK2-STAT5b signalling cascade is terminated by protein tyrosine phosphatase 1B (PTP1B).\textsuperscript{1-47} Inhibition of PTP1B exaggerates the signalling cascade, leading to accelerated DA production and DA receptor desensitization, such that the onset of lust is effectively reduced.

PTP1B can exist in either an inactive “open” or active “closed” conformation, which is determined by the catalytic WPD loop in the active site.\textsuperscript{55} In the closed state, the WPD loop allows the active site to dephosphorylate and terminate STAT5B activity.\textsuperscript{55} Upon allosteric inhibition, however, the open conformation of PTP1B is conserved, thus decreasing PTP1B catalytic activity.\textsuperscript{55} Allosteric regulators were chosen over orthosteric inhibitors, as they are easier to transport through cell membranes due to their small size, low molecular weight and reduced charge.\textsuperscript{59} The allosteric site is also easier to target as it is not well conserved and is significantly less polar than the active site.\textsuperscript{59}

In this study, the efficacy of three selective PTP1B allosteric inhibitors in reducing libido in human subjects was examined. These negative modulators included: 4-(aminosulfonyl)-7-fluoro-2,1,3-benzoxiadiazole (ABDF), Compound 2 (CPD2), and Nosexin.

ABDF inhibits PTP1B by reacting rapidly with Cys121, a cysteine residue located 10Å from the active site.\textsuperscript{28} By monitoring residual PTP1B activity for up to 2.5h, ABDF was found to attenuate 86% of PTP1B activity.\textsuperscript{28} CPD2 inhibits PTP1B activity by binding to Pro188 and Leu192, which are located 20Å away from the active site.\textsuperscript{55} This compound resulted in a rapid 70% decrease in PTP1B activity, with 90% reversibility.\textsuperscript{55} Aromatic rings added to the sulfonyl end of CPD2 gives it a unique lipophilic structure, thus increasing its selectivity and potency.\textsuperscript{55}
The newly-designed PTP1B negative allosteric regulator, Nosexin, was based on the pre-existing allosteric PTP1B inhibitors, ABDF and CPD2. Although these were originally designed to interfere with PTP1B associated with the insulin pathway\(^{28,55}\), Nosexin was developed by amalgamating their characteristics and modifying chemical substituents. These changes in structure are intended to make it specific to PTP1B involved in the prolactin pathway, and to maximize lipophilicity and selectivity for the Cys121 allosteric site. In vitro studies using high-throughput screening conducted in Amor Medical Lab conclude that in comparison to ABDF and CPD2, Nosexin has a greater binding rate and affinity for PTP1B, as well as a 93% ability to fully attenuate PTP1B functional activity. Its low molecular size and weight of 741.5 Da\(^{21}\) allows it to be used in a non-invasive intranasal spray, such that it can effectively bypass the blood-brain barrier and permeate through cell membranes to act intracellularly.\(^{49}\) In vivo studies conducted in our lab indicate that a 32.6 mcg/100µL dose of Nosexin significantly reduces copulatory behaviour and MPOA dopaminergic activity in 500 g rats. Dosage conversion using allometric scaling computes a human equivalent dose of 741 mcg/100µL for an average 70 kg adult male.\(^{21,43,46}\)

**Methods & Materials**

A double-blind study was conducted with 40 healthy and sexually-active heterosexual Caucasian males, aged 25-29 years. The participant parameters were restricted to eliminate confounding variables. This age group is found to engage most frequently in sexual behaviour\(^4\), making it a suitable choice to assess changes in libido, dopamine, and prolactin levels. This initial study comprises of people from the general population, as this is necessary before conducting clinical trials on sex offenders. Males were selected because 97% of convicted sex offenders in Canada are male.\(^7\)

Inclusion criteria required normal BMI, which is defined as the range between 18.5-24.9, as overweight/obese individuals can have abnormal sex hormone levels\(^{44}\) and exhibit sexual dysfunction.\(^{22}\) Participants were screened prior to the experiment to ensure that they were not currently taking prescription medications, so as to avoid drug interaction. Exclusion criteria included sleeping conditions, such as sleep apnea, as this has been highly linked to low sex hormone levels.\(^{41}\) Non-smokers, and those without a history of substance abuse, were selected for study since evidence suggests that tobacco can reduce libido and sexual performance.\(^{56}\) Ambient room conditions were maintained at 24 ± 1°C, and 40% relative humidity.

Dopaminergic activity of the MPOA was monitored using [18F]DOPA positron emission tomography (PET).\(^{53,58}\) Mental sexual arousal was monitored objectively using electroencephalography (EEG) by analyzing P300 brain waves. These originate from the parietal lobes of the brain, and are generated after receiving and integrating stimuli.\(^{52}\) Typically, the amplitude of P300 brain waves decrease upon viewing visual stimuli; however, the most drastic decreases in amplitude occur when the person is mentally aroused by sexually-stimulating images.\(^{11,52}\) P300 analysis is a recently-developed diagnostic tool currently used to assess the cognitive dimension of sexual arousal.\(^{11}\)
Experimental Testing

Subjects were divided into 4 equal groups consisting of 10 subjects each. All groups were assembled at 9:00 am and shown a 5-minute documentary on Canadian geography to establish baseline arousal levels. Following this, all individuals were shown an erotic film for 10 minutes. During the 10-minute period, dopaminergic activity in the MPOA was measured using PET. Simultaneously, mental arousal indicated by P300 brain waves was measured using EEG. Subjects were dismissed upon signing an agreement to not engage in sexual behaviour or strenuous activity for the next 24 hours.

At 9:00 pm of the same day, subjects were administered 741 mcg of a specific PTP1B inhibitor or placebo using a 100 µL intranasal spray. Group 1 was administered Nosexin. Group 2 was administered 4-(aminosulfonyl)-7-fluoro-2,1,3-benzoxiadiazole (ABDF). Group 3 was administered Compound 2 (CPD2). Group 4 was administered a placebo. The drug was given before sleeping in order to obtain maximal effect, as endogenous prolactin levels are highest during non-REM sleep.

Measurements of dopaminergic and P300 brain wave activity were repeated at 9:00 am the following morning during the second session. Alternate footage of the documentary on Canadian geography was shown for 5 minutes, followed by 10 minutes of erotic film.

Results

![Dopaminergic Activity in MPOA of Test Subjects Before and After Administration of Intranasal Spray](image)

**Figure 1.** Mean maximal dopaminergic activity ([18F]DOPA radioactive emission) observed in the MPOA by PET during a 10-minute screening of erotic film before and after administration of a randomly assigned drug/placebo. Nosexin (n=10, p<0.05) resulted in the largest decrease (53%) of dopaminergic activity, followed by ABDF (n=10, p<0.05) and CPD2 (n=10, p<0.05) in order of decreasing efficacy. Taking the placebo (n=10, p<0.05) did not result in a statistically significant decrease of dopaminergic activity compared to the first erotic viewing.
Figure 2. Mean percentage reduction in the amplitude of EEG-detected P300 brain waves when viewing 10 minutes of erotic film before and after administration of a randomly assigned drug/placebo. Each percentage reduction was calculated using the initial (baseline) and the mean P300 amplitudes achieved while the participants viewed erotic film. Participants taking Nosexin (n=10, p<0.05) exhibited the smallest decrease in P300 amplitude, indicating significant inhibition of sexual arousal. ABDF (n=10, p<0.05) and CPD2 (n=10, p<0.05) inhibited sexual stimulation to a lesser extent, while the placebo (n=10, p<0.05) failed to inhibit sexual arousal.

Adverse reactions to Nosexin reported by the participants were minor. These included bitter taste, minor irritation of the nasal cavity, pharyngolaryngeal pain, headaches and post-nasal drip. Symptoms subsided after 6 hours of taking the medication.

Analysis

As indicated by Figure 1, in comparison to PTP1B allosteric inhibitors ABDF and CPD2, Nosexin is most effective in reducing dopaminergic activity in the MPOA. Since the MPOA is responsible for regulating both the appetitive and consummatory aspects of lust, diminished dopaminergic activity suggests that libido was effectively attenuated. Figure 2 further validates this result, as Nosexin was able to significantly reduce cognitive sexual arousal and interest evoked from viewing erotic film. This is indicated by Nosexin’s ability to inhibit the large decrease in P300 wave amplitude normally observed when viewing erotic films without any lust-attenuating drug.

Justify Your Response

FUNSIN should continue to support our division, as Team Amor plays an integral role in precluding lust by implementing innovative pharmacological interventions. Lust is commonly recognized as one of seven deadly sins, and is a worldwide issue that has plagued humanity for centuries. While it carries a negative connotation with respect to personal morals, lust also poses significant ramifications on society’s well-being.
Lust can drive people to commit sexual offences, where severe physical and mental harm is inflicted. According to the United Nations, in 2009, there were 471 reported accounts of rape in Canada. However, this is an underestimate, as reported rapes comprise merely 6% of the total amount. This is especially alarming, as sex offender and incest recidivism rates within 15 years of the first offence are 37% and 13%, respectively. These values are significant once taking into account that 4724 male sex offenders were studied. Additionally, those with an overwhelming desire for sexual gratification may be more prone to making impulsive decisions, such as practicing unprotected sex. This would further contribute to instances of unintended pregnancy, abortion and sexually transmitted infections. As such, by eliminating lust, one can effectively reduce the occurrence of these repercussions in order to uphold the safety and health of society.

The proposed allosteric inhibitor, Nosexin, holds great promise for the treatment of lust, as it primarily functions to attenuate the desire for sexual gratification. Since it will be directly introduced into the CNS, Nosexin will interfere minimally with prolactin signalling cascades present throughout the remainder of the body; thus, lactation and reproductive function will remain unaffected. Evidence suggests that Nosexin will act predominantly in the MPOA, a region highly implicated in regulating appetitive sexual behaviour. This is due to especially high PRLR expression and STAT5b signalling in this region, thereby minimizing psychosis and motor dysfunction associated with significantly altered dopaminergic activity in the MLC and NS. Furthermore, since Nosexin was modeled after existing allosteric PTP1B inhibitors, CPD2 and ABDF, Team Amor has saved FUNSIN a significant amount of money and time in drug development.

Further studies must be conducted in order to validate the efficacy and safety of Nosexin in regards to the optimal dose required for reducing lust, without interfering with regular bodily functions. Though our study tested for side effects resulting from short-term administration of the drug, we must ensure that we identify all adverse effects that may occur due to extended intake, as well as withdrawal from Nosexin. Clinical trials that use a larger sample population consisting of our desired target audience, male sex offenders, will be conducted. This will help determine whether our results concerning Nosexin’s efficacy are consistent, or whether our drug should be discredited.

In the process of having this drug approved by the FDA and potentially marketed in North America, we must also conduct further pharmacokinetic tests to determine the shelf-life and half-life of the drug in the body. Nosexin’s metabolism must be tracked to ensure that it is broken down into non-toxic metabolites. Additionally, we must determine precisely how Nosexin interacts with drugs and alcohol. To accomplish these goals, however, adequate funding is necessary.

As demonstrated, the progress we have accomplished in such a short amount of time is phenomenal. However, a significant amount of testing is still required. We would be grateful for financial support in the development of Nosexin, a potential cure for lust.
**Acknowledgements**

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SECTION IV: ANNOTATED REFERENCES

* All diagrammatic representations embedded in the report are originally produced.*


This study details PTP1B’s mechanism of action in relation to STAT5a and STAT5b in prolactin pathways. It outlines all necessary information regarding these secondary messengers, including their specific mechanism of action and termination with respect to amplifying the PRL-induced response. This article proved useful, as it helped us decide which molecular step of the PRL pathway our drug would interfere with. It is a credible source, as it was published in a reputable peer-reviewed journal, and used rigorous experimental techniques in order to determine the functionality of STAT5 and PTP1B.


This journal compiles information from numerous studies and explores the involvement of various neuropeptides, such as oxytocin, in sexual behaviour. According to this journal, oxytocin has been found to facilitate sexual activity in rats, mice, rabbits, and humans. Intravenous administration of oxytocin in male rabbits reduced ejaculation latency and enhanced sexual stamina, indicating a facilitative role of oxytocin on sexual activity. Further, oxytocin antagonists given to rats diminished copulatory behaviour. This review article is credible, as it was published in a peer-reviewed journal, and uses copious amounts of referencing to support the statements made.


This article explores the role of oxytocin, also known as the affiliative hormone, in regulating anxiety and sexual behaviour. It provides extensive information on the synthesis and release of oxytocin. According to this article, oxytocin is produced in neurons of the supraoptic and paraventricular nuclei of the hypothalamus. The neurons project to the posterior pituitary, where oxytocin is released into the bloodstream. This article is credible, as it outlines an extremely detailed, yet clear procedure, and uses substantial data to generate well-presented graphs and autoradiographs that further validate their findings.
This 3-part study examines differences between the sexual peak for men and women. It was concluded that females reach sexual peak at older ages than males, and that the defining characteristic for ‘sexual peak’ was sexual desire and sexual satisfaction in males and females, respectively. This led us to select males for our study, who tend to exhibit more consistent sexual desire (lust) for their age. The age group shown to engage in intercourse most frequently was 25-29 years; thus, this was used as the age group of participants in the study we created in Section III. This article is credible, as it is published in a peer-reviewed journal of the International Association for Relationship Research. The study itself is written clearly such that it is easy to follow, and utilizes a fairly large sample size.

This article provides information about PRL base levels throughout the two sections of the sleep cycle: REM and non-REM. The results of the experiment indicated that circulating serum levels of PRL peaked during non-REM cycles in contrast to REM cycles. PRL is also shown to follow a sleep-dependent rhythm. This allowed us to identify the most ideal conditions for exaggerating PRL induced activity, and is why Nosexin should be administered immediately before sleeping. As a testament to this article’s credibility, it is cited by 6 other articles - all of which were published by professional peer-reviewed journals.

This article provides information about the properties and biological functions of the prolactin hormone and the distribution of its receptors. It briefly reviews the signal transduction pathways of the prolactin receptor, specifically the JAK2-STAT5 pathway. From this article, we acquired the knowledge that STAT1, STAT3, and mainly STAT5 are the three members of the STAT family that have been identified as signal transducer molecules of PRLR. It led us to understand that STAT5B is more specific in the regulation of dopamine levels. This article is credible, as it uses over 600 references to support its extensive, clear descriptions and diagrammatic representations of the JAK/STAT pathway. In addition, it has also been cited by 100 scientific articles.
This government document presents statistics and trend analyses on sexual assault cases in Canada. In our project, we decided to cater our drug to sex offenders. It is mentioned in this document that 97% of accused sex offenders are indeed male. As such, all of the participants selected in our study were male. Also, the majority of our research articles supporting prolactin-induced reductions in libido are valid, as they are performed on male human subjects and male rats. This source supports our claim that only 6% of rapes are reported to the police. This is a credible document, as it utilizes data from Statistics Canada.

This article discusses the relative distribution of STAT5, a specific class of signal transducer and activator of transcription (STAT) molecule. Prolactin-induced STAT5 is associated in areas of the brain that contain prolactin receptor mRNA, except for the paraventricular nucleus and median preoptic nucleus. The relative abundance of STAT5 is distributed among other areas as well. Specifically, the rostral and mediobasal hypothalamus contain the highest accumulation of STAT5. This region includes the medial preoptic area (MPOA), which prompted us to infer that a PTP1B inhibitor would act predominantly in the MPOA due to the high amount of STAT5 activity it would inhibit. This article is credible, as uses appropriate referencing techniques and is cited by 4 other scientific papers. It also presents clear legends to accompany its figures, making it easy to interpret regions of high STAT5b radioactive labelling in various areas of the brain.

This review article identifies the definite correlation between sexual dysfunction and hyperprolactinemia (HPRL) in men. It is proven that the increase in tyrosine hydroxylase mRNA expression in the hypothalamic arcuate and periventricular nuclei (regions that regulate sexual and erectile function) is caused by hyperprolactinemia. Chronic hyperprolactinemia results in a down-regulation of dopamine receptors, leading to inhibition of libido. This article cements our understanding about the actions of PRL on attenuating dopaminergic activity and provides proof that PRL is effective in decreasing libido. This journal is credible, as it is cited by more than 30 other articles and utilizes data from 3200 patients.
This study utilizes in vitro immunologic techniques to demonstrate the activation of JAK2 by PRL receptor stimulation in the mice mammary gland. This allowed us to narrow our focus on JAK2 pathways specifically, as manipulating this amplification cascade is the key to exaggerating the PRL response. This article is credible, as it has been cited by 21 other articles in PMC. It also utilizes a significant amount of quantitative data to support its conclusions.

This paper discusses new developments made in electroencephalography (EEG) testing as a means to study the cognitive aspect of sexual stimulation. This advanced neuroimaging tool detects P300 brain waves down to the millisecond. Analysis of the amplitude of P300 brain wave activity is proven to be a consistent indicator for sexual interest. 30 healthy volunteers were exposed to various video clips, including erotic films. Using EEG analysis, it was determined that arousal generated the greatest decrease in P300 brain wave amplitude. These results were in agreement with the participants’ self-reported levels of libido. The article, however, reveals that it is difficult to differentiate forms of arousal from the P300 waves, such as distinguishing between terror and sexual stimulation. The paper is credible, as the study conducted was well-controlled. Further, it is an extremely recent article that contains up-to-date information.

This paper demonstrates the ability for prolactin to activate tyrosine hydroxylase, a rate-limiting enzyme involved in the synthesis of dopamine. Within one to four hours, PRL was found to stimulate excessive dopamine release in the mediobasal hypothalamic, nigrostriatal and mesolimbic pathways of male rats. Thus, acute hyperprolactinemia has the potential to temporarily increase dopamine effects due to exaggerated TH activity. This may, in turn, facilitate sex drive. For this reason, we proposed for our drug to be used as a chronic treatment plan, with regular doses taken immediately before sleeping in order to avoid lustful behaviour while DA levels are elevated. This is a valid source, as it is published in a reputable journal and is cited by 8 other scientific papers.

This article explores the effects of cabergoline treatment, a dopamine agonist, in men with prolactinomas (prolactin-secreting tumors). Cabergoline was effective in treating both sexes with prolactinomas, as dopamine can act in tuberoinfundibular regions to negatively regulate PRL release. This study provided useful criteria and data that strengthened the inverse relationship between elevated prolactin levels and libido. Male participants with serum prolactin levels exceeding 200µg/L due to macroprolactinoma growth reported significant libido impairment and testosterone deficiency. This study is credible, as it comprised of a fairly large sample population of 102 people. Further, it is cited by 10 other papers.


This study explores the effect of cyproterone acetate, an androgen antagonist, in reducing sexual interest in men. It is noted that this compound significantly reduces physiological features of libido, such as erection, as opposed to the psychological component of sexual motivation. This drug was also tested in a prison setting, where cyproterone acetate reduced serum testosterone levels by 30%, subsequently attenuating libido. The author suggests for this AR antagonist to be used when treating sex-offenders. This article is credible, as it is published in a peer-review journal and utilizes clear, appropriate tables and graphs to validate its conclusions.


This study examines the impact of serotonin reuptake inhibitor (SSRI) medications on sexual dysfunction. Three detailed case studies show that patients taking these medications report low libido, anorgasmia, genital anesthesia and erectile dysfunction. It is explicitly stated that it was previously assumed that these side-effects would resolve once the treatment was over. However, there have been several incidences in which sexual dysfunction persist even after discontinuing treatment. This is a significant drawback; thus, it provided rationale as to why serotonin was eliminated as a potential molecule to target. This is a credible article since it was published in a peer-reviewed scientific journal and appropriate references other articles to validate its conclusions.
This textbook contains a chapter exploring signal chemicals involved in the maintenance of homeostasis, with a focus on sex hormones. It outlines, using diagrams and clear descriptions, the role of the hypothalamus and pituitary in releasing LH and FSH in order to regulate the production of estradiols and androgens that are crucial to the physiological components of sexual function. This provides basic knowledge on the molecular pathways behind libido, and shows how complex the interactions between various hormones truly are. This is a credible source, as it is a published textbook that is distributed in schools across Ontario for educational purposes in the subject of biology.

This review paper explores the effects of DA antagonists, agonists and lesioning on sexual function in the MPOA, which is suggested to be involved in regulating anticipatory sexual behaviour and the initiation of copulation. D1 and D2 receptors in the MPOA are primarily involved in mediating the anticipatory and consummatory features of libido. The use of DA antagonists in the MPOA significantly decreased the percentage of times that male rats approached a receptive female. For our purposes, this paper demonstrates the clear relation between decreased dopaminergic activity in the MPOA and inhibition of sex drive. Thus, Nosexin, which acts predominantly in the MPOA should be effective in reducing libido. This paper is credible, as it uses a significant number of references to support its claims, and has been cited by 86 other articles.

This paper addresses the phenomena of increased sexual behaviour as a result of acute hyperprolactinemia, and offers speculation on the long-term effects of hyperprolactinemia in the male rat brain. It performed studies on a randomized sample of rats. These revealed that acute hyperprolactinemia can facilitate sexual behaviour, including mounting and grooming. In the long-term, however, this behaviour disappears due to chronic hyperprolactinemic. As such, it is hypothesized that prolonged prolactin-induced stimulation of dopamine receptors results in hyposensitization, thus contributing to lowered dopaminergic activity and the inhibition of lust. The study is credible, as it utilizes proper experimental controls, and is published in a peer-reviewed journal.
This study examined the effects of subcutaneous injections of prolactin at low dosages in male and female rats. Though it has been well-established that chronic hyperprolactinemia inhibits sexual behaviour, it was found that elevating serum-prolactin levels by small amounts significantly increases the frequency of mounting, intromission and ejaculation. Specifically, 5, 10 and 50 μg/kg doses of PRL were administered, which subsequently elevated serum-PRL levels to 50-200 μg/L. The lower concentration of this scale falls within normal physiological levels, such as that seen after orgasm. None of the doses were able to reduce copulatory behaviour in normal, healthy rats. However, the 50 μg/kg dose did inhibit copulation in impotent rats. This study is credible, as it is published in a reputable peer-reviewed journal and is cited by 16 other scientific papers.

This study uses male rat brain lesions to determine which areas are primarily responsible for sexual motivation. A preference test was used to measure the sexual motivation of male rats, which involved the use of a testing area consisting of a male rat, a sexually receptive female, and a non-receptive female. Lesions of the medial preoptic area (MPOA) and the dorsolateral tegmentum (DLT) in the male rat decreased the amount of time spent with a sexually receptive female, thus showing a decrease in sexual motivation, or libido. It was therefore concluded that the MPOA and DLT have similar and significant roles in regulating sexual motivation. Thus, Nosexin should be effective in decreasing libido as it mainly acts on the MPOA. This study ensures its maintenance of control variables, and is published in a reputable journal. It has been cited by 52 scientific papers, thus validating its reliability.

EMD Millipore offers chemical information on various drugs. This particular webpage offers product data on a selective cell-permeable allosteric PTP1B regulator that inhibits enzymatic activity by preventing closure of the WPD loop. Its molecular weight is 741.5 Da, with a dosage concentration of 2mg/270μl. As such, Nosexin’s properties and dosage were based off of these values. This is a credible source, as EMD Millipore Chemicals is a professional company that is at the forefront of scientific research, development and technology in America.
This review paper examines the existence of a relationship between being overweight/obese and erectile dysfunction (ED). Results found that increased BMI can elevate the risk of ED by 30-90% in comparison to control subjects. Moreover, sexual dysfunction was more prevalent in overweight and obese women. Thus, by choosing to have healthy participants within a normal BMI range in Section III, we remove the potential risk of having overweight subjects with erectile dysfunction. This could potentially cause discrepancies in the efficacy of our drug. This study is credible, as it utilizes properly and clearly labelled figures that support its claims, and is cited by 31 other scientific papers.

This document outlines the precautions and side effects associated with taking PATANASE, an H1 antagonist used for treating seasonal allergies, in the form of intranasal spray. It includes results of a 2-week clinical trial, outlining the side-effects reported by participants as a result of taking the medication through the nasal cavity. The most common adverse reactions were included in the analysis section of our study, as these may be short-term side effects that are most likely to result from taking Nosexin. This is credible, as the FDA, which approves the distribution of drugs in the United States, published this document. Also, a large patient sample (n=2992) ranging from children to adults was studied.

This longitudinal study explores the implications of low testosterone and estradiol levels with respect to bone health. 2447 healthy men over the age of 65 years were selected for analysis. It was concluded that deficiencies in the two aforementioned sex hormones conferred a significantly greater prevalence of hip bone loss and osteoporosis. As such, we inferred that manipulating testosterone and estradiol levels in the body would have deleterious effects, and that the risks would outweigh the benefits of decreasing libido. This is a credible study, as a large sample population was analyzed. It was also written by multiple authors from various professional institutions, and is published in a reputable peer-reviewed journal.

This article provides general information about the polypeptide hormone prolactin. It mentions the synthesis process of prolactin, properties of the prolactin receptors, and its biological significance. The JAK2/STAT pathway of prolactin is also described in detail. This article provides a general idea of the structure, function, and regulation of prolactin, helping us to better understand the prolactin hormone, as well as helping us identify potential loci for intervention. This article is credible, as it supports its information with 1926 references. It has also been cited by 100 other articles and is published by a reputable group, titled the American Physiological Society.


This thesis paper explores the impact of oxytocin antagonists on sexual behaviour. When these were administered intracerebroventricularly in male rats, the rats displayed decreased penile erection, frequency of intromissions and ejaculation. It is thus evident that oxytocin plays a significant role in regulating the physical aspects of sexual behaviour. However, this paper explicitly states that additional research needs to be conducted to determine the role of oxytocin in promoting sexual motivation in the MPOA, our main target for reducing lust. Thus, this made oxytocin a non-viable target for targeting lust. This article is credible, as it is an extremely recent paper that utilizes up-to-date information. It includes a biographical sketch of the author, who has outstanding academic standing and has been writing peer-reviewed scientific papers and delivering several presentations related to this topic since 2001. Further, it was approved by Elsevier, a reputable medical and health science publisher.


This paper attempts to explore libido using biological reductionism. Defined as sexual motivation, libido is divided into two main components: sexual arousal and sexual desire. These are mediated by a complex interplay of neuroendocrinological signals and sensory signals, all of which regulate physiological genital function and psychological stimulation. The article gives a brief overview on each of the five human senses, and describes how different forms of sensory input can contribute to sexual stimulation. This document is credible, as it is cited by 11 other scientific papers, and uses extensive referencing to validate its information.
This paper provides information about ABDF, a molecule that allosterically inhibits PTP1B by selectively modifying a cysteine residue (Cys121) located 10Å from the Cys215 active site. It highlights the properties of ABDF, such as its selectivity, efficacy, and reversibility. These properties established a basis for Nosexin’s molecular characteristics and properties. Furthermore, the efficacy of ABDF (86%) aided us in determining the relative decrease in amplitude of the P300 graph and the relative decrease in dopaminergic activity for ABDF in comparison to Compound 2 and Nosexin. For example, since ABDF has a higher efficacy than Compound 2, it has a lower percentage decrease in P300 wave amplitude, as well as lower dopaminergic activity than Compound 2. This article is credible, as it utilizes a clearly detailed in vitro experimental design, with numerous controls. It also presents its data in graphs accompanied by clearly-described legends. Also, it is published in a peer-reviewed journal under a reputable group, the American Chemical Society.

This document reviews a 20-year longitudinal study done on sex offenders, and is designed to analyze rates of recidivism. Though the majority of rapists, child molesters and incest offenders are not accused of committing another sexual offence after their first crime, there is still a significant percentage that does not follow this trend. Data presented in this critical analysis show that sex offender recidivism is still an issue in Canada, and thus, if a drug could cure lust in such people, Canada might become a safer place. This document is credible, as it utilizes a large sample of 4724 male sex offenders, and is created in conjunction with the Canadian government.

This webpage provides information on serotonin syndrome, which results from excess endogenous serotonin. This is a potentially life-threatening condition, resulting in a variety of symptoms, such as increased heart rate, hallucinations, nausea, and a loss of coordination known as ataxia. This information is credible, as MedlinePlus is a trusted health information site that provides access to information from the US National Library of Medicine and the National Institutes of Health. It was last updated by an MD in June 2010, and offers a reference list.
This in vitro study examined the effects of intracerebroventricular (i.c.v.) injections of prolactin (PRL) on the activity and sensitivity of dopaminergic neurons in the mesolimbic and nigrostriatal pathways, and on the in vitro release of dopamine (DA) and 4-dihydroxyphenylacetic acid (DOPAC) in perfused striatal fragments. In the mesolimbic system, prolactin administration to normoprolactinemic rats decreased DA/DOPAC contents and D1 receptor density. The inhibitory effect of peripheral PRL on the nigrostriatal and mesolimbic dopaminergic neuronal systems was demonstrated. This paper's credibility is supported by the thorough discussion of the results obtained. This included pointing out potential errors in their experiment and future plans. It also utilizes a significant number of sources to support its conclusions.

This study demonstrates that estrogen plays a significant role in the maintenance of cardiovascular health. As such, we inferred that lowered testosterone levels that would decrease estrogen synthesis would result in increased risk of atherosclerosis. This is a credible study, as its experimental design of being a double-blind, randomized and placebo-controlled study is best for avoiding bias. It also uses extensive statistical analysis to generate a well-supported conclusion.

This in vitro study explores the desensitization of the wild and mutant types of dopamine receptors as a result of exaggerated dopamine effects. After 1 hour of dopamine pretreatment, the wild-type receptor (found in the body) exhibits 80% desensitization. This supports the hypothesis that extended periods of excessive dopamine release in the NS, MLC and MPOA can ultimately result in decreased dopaminergic cAMP response and inactivity due to receptor desensitization. This is a credible source, as the study detailed how it maintained control variables, and also presented its findings is numerous clear, well-labelled graphs. Further, it is published in a reputable peer-reviewed journal.
This paper characterizes sexual activity as a neuroendocrinological phenomenon that is dependent on levels of endogenous prolactin. This hormone modifies dopamine release in the nigrostriatal and mesolimbocortical regions - areas responsible for genital responses and regulation of sexual desire. The study investigates the effects of 50 microgram injections of prolactin on sexual arousal in ten males, under three subscales - appetitive, consummatory, and refractory. A decrease in PRL levels caused an increase of sexual drive. However, short-lived increases in prolactin resulted in minimal reductions of ~10% in the participants’ rating of their own appetitive and consummatory sex drive levels. The study also served as inspiration for our own methodology, as they too used erotic videos to induce sexual arousal in subjects. The paper’s thorough description of its methods, clearly labelled graphs, and discussion of potential error or objectivity in the experiment renders this a credible source.

This paper investigates the role of prolactinergic and dopaminergic systems in the regulation of sexual behaviour. It provides an in-depth discussion of the interactions between these two systems and supports its findings with recent experimental and clinical studies. While dopamine agonists enhance sexual behaviour, chronic elevations in prolactin (PRL) inhibit appetitive sexual behaviour. This study identifies the medial preoptic area (MPOA) as one of the most significant areas controlling the motivational and consummatory components of sexual behaviour due to its strong expression of PRL receptors. An increase in PRL in the MPOA decreases dopaminergic activity. Sexual behaviour is also mediated by the mesolimbocortical and the nigrostriatal dopamine pathways, which regulate the motivational and sensorimotor aspects of sexual behaviour, respectively. This paper reviews recent papers and uses extensive referencing to support its findings, thus deeming it a credible source.

This paper introduces the presence of dopamine receptors not only in the central nervous system, but also in the cardiovascular system. Peripheral dopamine receptors are found to be located on vascular smooth muscle and renal cells, as they regulate vasodilation and diuretic responses. They are also involved with the release of aldosterone from the adrenal cortex. Thus, we have concluded that
interfering with dopamine levels and receptors body-wide would produce many undesired adverse effects. This article is credible, as it is cited by 178 other scientific papers, and utilizes thoroughly supported details from hundreds of references in order to describe the various functions of dopamine receptors.


This article states that prolactin specifically activates STAT5B in neuroendocrine dopaminergic neurons. It demonstrates that STAT5b selectivity was confirmed in vivo, where the injection of prolactin in bromocriptine-treated rats stimulated a time-dependent increase in STAT5b, but not STAT5a. From this, we concluded that the signaling pathway involves the regulation of prolactin in dopaminergic system is JAK2-STAT5b. This article is credible because it is published by The Endocrine Society, which is the foremost professional society serving the endocrine community. In this article, the results of many experiments are shown in terms of clear data and diagrams. This article was published relatively recent.


This review paper focuses on the importance of the dopaminergic system in male sexual functioning. D1 and D2 receptors in the incertohypothalamic system and nigrostriatum facilitate sexual performance, such as erection, while the mesolimbic and pre-optic area regulate sexual desire, motivation and reward. Destroying the MPOA dopaminergic system with 6-OH-DA resulted in a 200% increase in mount and ejaculation latencies in rats, thus showing that low dopamine levels result in low sexual drive and activity. The relationship between DA levels and hormones, such as serotonin, oxytocin, testosterone and prolactin, was explored. In particular, it is discussed that short-term hyperprolactinemia fails to reduce copulatory behaviour, while chronic hyperprolactinemia is highly correlated to decreased libido. The credibility of this article is supported by its extensive use of referencing from 199 sources. It was cited by 55 other papers.


This journal is a compilation of 298 studies and provides extensive information on how various hormones and neurotransmitters play crucial roles in regulating libido. For instance, oxytocin is involved in major processes, such as attachment, maternal bonding and lactation. We did not want to interfere with these processes by decreasing oxytocin levels in order to reduce lust. This review also
discusses testosterone’s ability to increase libido in hypogonadal men and post-menopausal women; however, it reveals that there is inconsistent evidence supporting its ability to induce the same effects in pre-menopausal women. With respect to serotonin, this journal states that serotonin exerts a stimulatory effect on sexual functioning when acting on 5-HT1A receptors and an inhibitory effect when it acts on 5-HT2/5-HT1B/5-HT1C receptors. When selective serotonin reuptake inhibitors are given to subjects to increase serotonin activity, a decrease in libido and sexual dysfunction was observed. This journal is credible, as it is a monthly peer-reviewed journal published by the American Medical Association.


This study explored the effects of dopamine agonists and antagonists on the medial preoptic area (MPOA) and nucleus accumbens (NAcc) in male rats. Sexual motivation was determined by observing the behaviour of male rats in an X-maze made up of four boxes containing a male rat, a receptive female rat, or neither. Dopamine receptor antagonism in the MPOA decreased the number of times the female’s box was chosen, showing reduced sexual motivation. Similar tests indicated that the NAcc did not affect sexual motivation. Rather, this region appears to have greater influence on the sensorimotor aspects of copulation. This paper is a credible source, as it has been cited 19 times and provides detailed observations on the effect of each dopaminergic agonist and antagonist used.


This study examines how low levels of sex hormones are a suspected risk factor for sleep-disordered breathing. Findings show that women classified as having sleep apnea by the apnea-hypopnea index (greater than 10 hours of sleep) had significantly lower levels of sex hormones, including progesterone and estradiol. This prompted us to select individuals with no history of sleeping conditions for our experiment in Section III, as lowered sex hormone levels may impair libido and produce error or bias in our results. This study is credible, as it is cited by 7 other articles, and is published in conjunction with the International Journal of the Science and Practice of Sleep Medicine, which peer-reviews its publications.


This in vitro animal study investigates how D1 and D2 antagonists function to modulate sleep cycles in rats. It was found that REM and non-REM duration were modified, with REM cycles being shorter than usual. Meanwhile, non-REM
was altered depending on which receptor the DA antagonist acted on. As such, interfering with dopamine in the brain poses the risk of changing one’s normal sleep patterns, which is a reason why we chose to avoid using DA antagonists as our anti-lust treatment. The study presents a significant amount of quantitative data, and identifies potential error in its results. This paper was cited by 43 other sources, a true testament to its credibility.


This article discusses the use of intranasal sprays for the delivery of small-molecule drugs into the central nervous system, such that they can bypass the blood-brain barrier through non-invasive means. Drugs should be lipophilic to optimize their ability to diffuse through the arachnoid membrane into the olfactory CSF. Additionally, this paper notes that the human nasal cavity can maximally withstand 100µl per nostril without local injury. This supports our rationale for limiting the spray volume to 100µl. This is a credible source, as it has been cited by 49 other scientific papers, and utilizes extensive referencing to support its claims.


This article explores the relationship between body composition and sex hormone levels in premenopausal women. Obese women, who have a BMI greater than 30, have greater levels of testosterone and lower levels of estrogen than control subjects. In order to determine the effectiveness of our drug in reducing libido, we chose not to have obese individuals as test subjects, for abnormal hormone levels may have altered the consistency of our results. This led us to select individuals whose BMI fell within the normal range of 18.5 - 24.9 for our study. This study is credible since it is cited by twenty-two other articles and is published in a reputable peer-reviewed journal.


This study investigates various dopamine antagonists and their ability to attenuate both the appetitive and consummatory aspects of libido. It is noted that D1 and D2 antagonists, such as those used in antipsychotic medications, effectively decrease the frequency of mounts and orgasm achieved by male rats. High doses of 20 mcg of haloperidol that were injected directly into the MPOA entirely ceased copulation in rats. This study was useful as it proved that dopamine antagonists are effective in reducing libido, thus attenuating lust. This
is a credible paper, as it is published in a reputable journal and is cited by 220 other studies.


This article offers a comprehensive overview on how animal doses can be translated into a human equivalent dose using allometric scaling. The equations required for this conversion are given, and the scaling constants are noted for various animals, including rats, rabbits, monkeys and hamsters. We utilized these to calculate the conversion of a human dose to a rat dose for our drug, Nosexin. The paper is credible as it bases its information from current FDA guidelines.


This article provides an extensive amount of information on the cytokine signalling transduction pathways, which consist of JAK and STAT proteins. These signaling cascades are regulated by various termination mechanisms. These include numerous enzymes, such as SOCS, CIS, PTP and PIAS, which act on specific forms of JAK and STAT that are detailed in the article. Additionally, ubiquitin and proteasome degradation are explained in great detail. Through this, we were able to narrow down our target to PTP1B since it selectively regulates JAK2 and STAT5b proteins, the two components of PRL signalling. This article utilizes tremendously clear diagrammatic representations to summarize its information. Further, it supports its claims from 142 sources. 156 other scientific articles have cited this article, indicating its credibility.


This article discusses the potential issues associated with overstimulating the prolactin receptor. Through performing an in vitro experiment on human embryo kidney cells, it was found that treatment with exogenous prolactin promoted the degradation of the prolactin receptor via endocytosis and ubiquitination. This allowed us to conclude that introducing exogenous prolactin or prolactin agonists is a method inferior to our drug mechanism. The study itself is well-structured, clear in its descriptions and provides graphs and legends that are easy to analyze. This article is credible, as it was recently published in an accredited scientific journal after approval by an international editorial board. Multiple authors from varying reputable institutions contributed to this paper.
This review paper explores the effectiveness of intranasal spray use with regards to delivering drugs directly to the CNS, such that the blood brain barrier can be bypassed. It provides information on the characteristics that drugs must have in order to be administered through an intranasal spray. For instance, the maximum molecular weight of the drug permitted is 1000 Daltons. Therefore, Nosexin, which has a molecular weight of 741.5 Da, can be given to the target audience through an intranasal spray device. This paper is credible since it utilizes extensive and proper referencing, and is published in a reputable journal.

This 15-year study explores the strength of the relationship between serum testosterone levels and libido in 1632 men aged 40 to 70 years. It was explicitly stated that there was minimal difference between serum-T levels in men reporting decreased sexual drive and those without, suggesting that other hormonal factors play a more important role in regulating libido. The study concludes that this weak correlation indicates that one’s endogenous testosterone level is not a determining factor of sexual motivation, particularly in healthy men who do not suffer from hypogonadism. This paper is credible, as it utilizes a large sample population and identifies biases and potential errors in the study.

This spreadsheet outlines data on the number of crimes committed, by country, on an annual basis from 2003 to 2009. It is further divided by classifications of crime. Statistics referring to reported account of sexual offences, namely rape in Canada, were utilized in the proposal justification to strengthen the importance for pursuing our research. These numbers demonstrate how lust can cause severe consequences with respect to the sense of security in Canada. This is a valid source, as it comes directly from the United Nations Office on Drugs and Crime, which receives the information from annual international surveys.
This paper discusses the connection between P300 brain waves and sexual arousal. By analyzing 30 subjects, it was found that a greater decrease in amplitude of P300 waves was strongly indicative of increased sexual arousal. We used this research as a means of determining an objective testing method for sexual interest in subjects while viewing erotic film. The measurement of percentage decrease in P300 wave amplitude served as our y-axis for Figure 2 in Section III. Also, percentage decrease in P300 wave amplitudes prior to intranasal spray administration in our study was obtained from the higher values in the scatter plot included in this paper, which showed an 80% amplitude decrease after being mentally aroused by sexual content. Percentage decrease in P300 wave amplitudes for Nosexin was obtained from the lower values (~15%) of the scatterplot to indicate minimal sexual arousal. The percent decreases in P300 amplitudes for ABDF and Compound 2 were placed in between 15% and 80% to represent their relative efficacies. This study is credible, as it was published in association with the American Urological Association, and clearly outlines its controlled experimental procedure and results.

This review article explores how PET is used to monitor the activity of dopaminergic neurons and the dopamine system by tagging dopamine, dopamine precursors, and dopamine receptors. It provided us the experimental method for using PET to monitor changes in dopaminergic activity in our test subjects before and after administering intranasal drugs/placebo. This article comes from a reputable journal and is a reliable source, as it uses 254 sources to support its information.

This review article demonstrates the role of JAK/STAT pathway and reviews the signal induction of prolactin. It supports the concept that the intracellular components involved in generating an effect by prolactin entail the JAK2-STAT5 secondary messenger system. In order to select our loci for intervention and develop our drug, this basic information on the prolactin signal cascade and transduction was necessary. The article utilizes clear and concise diagrammatic
illustrations of the PRL signal cascade. It is credible since it has been recently cited by 10 other articles and is published by a reputable source.


This paper provided information regarding a novel allosteric site located 20Å away from the active site. It highlights the mechanism of the catalytic WPD loop in PTP1B inhibition. The research provided greater understanding of Compound 2, a type of allosteric PTP1B inhibitor, which helped us understand the structure and function behind PTP1B allosteric regulation. This aided in the molecular development of Nosexin as an effective PTP1B inhibitor. Furthermore, the article discussed the efficacy of Compound 2 (70%) in PTP1B inhibition. This aided us in determining the relative decrease in amplitude of the P300 graph and the relative decrease in dopaminergic activity in the PET graph for this inhibitor compared to the other two PTP1B inhibitors, ABDF and Nosexin. It was assumed that the relative efficacy of Compound 2 compared to that of Nosexin and ABDF would correlate to the relative percentage decrease in P300 amplitude and relative decrease in dopaminergic activity in the MPOA. For example, Compound 2 has lower efficacy than ABDF, and thus would have a greater percentage decrease in P300 wave amplitudes and greater dopaminergic activity than ABDF. The study was published as part of the well-established academic journal, Nature.


This study investigates the effect of nicotine from cigarette smoking on increased levels of sex hormones. Results have shown that nicotine causes increased endogenous levels of circulating cortisol, growth hormone, and prolactin in males through a study involving increasing doses of nicotine. As a result, we have chosen to select non-smokers and those without history of substance abuse since such people may have altered sex hormone levels that may make it difficult to achieve consistent and accurate results on libido reduction. This study is credible since it is cited by 40 scientific studies, and is published by an internationally-recognized peer-reviewed journal.


This study investigates the cause-effect relationship between low dopamine and neuropsychological conditions, with an emphasis on depression, Parkinson’s and
Alzheimer’s. Low levels of dopamine were found to be associated with slow sensori-motor task performance, deficits in verbal fluency and impaired short-term memory. This forms the basis of our conclusion that manipulating dopamine levels to reduce lust in the NS and MLC would pose too much risk to their long-term well-being. The paper is credible, as it is able to offer quantitative data on the patient’s skill sets. It is also cited by 33 scientific articles.


This paper examines abnormal dopamine activity in patients with bipolar disorder and mania. The experiment was conducted with PET, using the radioisotope [18F]DOPA. In this study, dopaminergic activity indicated by radioactivity was measured in megaBecquerels. This served as the y-axis for Figure 1, Section III in our report. This study also provided the correct dosage of radioactive dopamine (185 MBq) to administer to subjects when testing for the PTP1B inhibitors’ effects on dopaminergic activity in the medial preoptic area. It was assumed that ~185 MBq of [18F]DOPA would be seen in baseline dopaminergic activity, and that a reduction in dopaminergic activity due to desensitization of DA receptors in the MPOA would result in decreased radioactivity captured by the PET. This article is credible, as it was published in a reputable journal, was written recently, and had numerous contributing authors.


By discussing the recent efforts made to find a PTP1B inhibitor for insulin, this review evaluates the potency and selectivity of a variety of PTP1B inhibitors, and discusses strategies to consider when creating these inhibitors. Among the evaluated inhibitor types are bidentate ligands and allosteric inhibitors. Bidentate ligands engage both the active and adjacent site, and exhibit high specificity and affinity. Allosteric inhibitors are cell permeable, low-charge, small molecule inhibitors that target allosteric sites on PTP1B. Nosexin was modelled after the allosteric inhibitor type. This article was published in *Drug Discovery Today*, a peer reviewed and reputable digital scientific magazine. Furthermore, it was cited 143 times by other scientific publications, rendering it a credible source.