

REVIEW ARTICLE



Nitric Oxide, Humming and *Bhramari* Pranayama

B P Ushamohan^{1*}, Aravind Kumar Rajasekaran²,
Yamini Keshavaprasad Belur², Judu Ilavarasu¹, T M Srinivasan¹

¹ Division of Yoga and Physical Sciences, Swami Vivekananda Yoga Anusandhana Samsthana (S-VYASA), Bengaluru, India

² Department of Speech Pathology & Audiology, National Institute of Mental Health and Neurosciences, Bengaluru, 560 029, India

 OPEN ACCESS

Received: 08-06-2022

Accepted: 20-07-2022

Published: 11-02-2023

Citation: Ushamohan BP, Rajasekaran AK, Belur YK, Ilavarasu J, Srinivasan TM (2023) Nitric Oxide, Humming and *Bhramari Pranayama*. Indian Journal of Science and Technology 16(5): 377-384. <https://doi.org/10.17485/IJST/v16i5.1212>

* Corresponding author.

ushamohanbengaluru@gmail.com

Funding: None

Competing Interests: None

Copyright: © 2023 Ushamohan et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Published By Indian Society for Education and Environment ([iSee](https://www.isee.org/))

ISSN

Print: 0974-6846

Electronic: 0974-5645

Abstract

Background: Nitric Oxide has been recently recognized as an extremely important molecule in biophysics that has a profound role in the regulation of various functions in the body. It is abundant and continuously replenished in the paranasal sinuses of the respiratory system in healthy adults. Studies have demonstrated that nasal Nitric Oxide levels in the airways increase multi-fold during humming compared to quiet nasal exhalation. Humming during exhalation is an integral part of *Bhramari Pranayama*. **Objectives:** This review is to understand how humming is associated with Nitric Oxide production, and evaluate the suitability of *Bhramari Pranayama*, and the classical version of *Bhramari Pranayama*, which has humming as its integral part, for the application of maintenance of the airway integrity. **Method:** We have searched relevant current scientific literature pertaining to Nitric Oxide, voice production especially humming. We also reviewed the classical yoga texts where *Bhramari Pranayama* is elaborated. We tried to correlate how *Bhramari Pranayama* may help to endogenously produce Nitric Oxide and thereby regulate various respiratory functions. We made special efforts to distinguish between general and classical versions of the practice of *Bhramari Pranayama*. **Findings:** Experimental evidence suggests that humming significantly influences Nitric Oxide production. *Bhramari Pranayama* which has humming as its integral part may therefore facilitate Nitric Oxide production endogenously, both during inhalation and exhalation, and thereby help in the regulation of respiratory processes. **Novelty:** Research to date, has been done on increased expression of Nitric Oxide during humming (during exhalation). The classical version of *Bhramari Pranayama* which also includes humming during inhalation also known as inhalation phonation, alternating with humming during exhalation seems to offer a wholesome solution for increased stimulation of Nitric Oxide as well as the optimal end use of the much sought-after molecule.

Keywords: Nitric Oxide; Humming; *Bhramari Pranayama*; Para Nasal Sinuses; Inhalation Phonation

1 Introduction

Nitric Oxide (NO) is a remarkably simple component which has received a great deal of attention for its versatility and importance as a key intracellular and intercellular signaling molecule. It is endogenously generated in mammalian cells and regulates a range of physiological and pathophysiological mechanisms. Previously, it was considered as an atmospheric pollutant with no biological role. However, it was demonstrated independently by Ignarro et al., and Palmer et al.,⁽¹⁾ that the endothelial-derived relaxing factor (EDRF) released from the vascular walls was essentially NO. This led to the possibility that NO might have a role in our biological systems and enthused further research that has led to a plethora of discoveries. In 1992, Nitric Oxide was named "the molecule of the year" and in the year 1998 Furchgott, Ignarro, and Murad were awarded Nobel Prize for their discoveries concerning NO as a signaling molecule in the cardiovascular system.

NO is involved in several regulatory, protective, and defensive processes and is also secreted in response to inflammatory processes. It acts as a powerful vasodilator that relaxes the smooth muscle fibers of the vascular wall. It regulates blood vessel tone; it functions as a biological mediator comparable to neurotransmitters in the neural system. It acts as an important host defense in the immune system and also acts as a cytotoxic agent in the pathological process, particularly in inflammatory diseases. NO is produced by various cells throughout the body including the respiratory airways. Recent pathbreaking research by Weitzberg and Lundberg demonstrated that nasal Nitric Oxide levels in the airways increase considerably during humming compared to quiet nasal exhalation⁽²⁾. Taking into consideration the efficacy of NO in the regulation of various crucial mechanisms, the application of humming has been emphasized for its remarkable capacity to proliferate NO availability. It is an interesting observation that humming is an integral part of *Bhramari Pranayama*, (BhPr) an ancient yogic breathing technique.

This review is about understanding the application of humming in the expression of NO in the airways and its role in regulation of various functions in the respiratory system. We review certain experiments made on the basis of acoustic background of humming that enhance the NO expression in the paranasal sinuses. We also make an effort to evaluate the suitability of BhPr for its ability to enhance the NO expression in the paranasal sinuses. According to the ancient yoga text Hatha Yoga Pradeepika, BhPr is producing a humming sound, at a sustained low pitch, depicting a female bumblebee. Adding the dimension of acoustics to breathing in BhPr, make it unique among other pranayamas. The humming sound is produced during exhalation after a controlled inhalation. This variation of BhPr is done as a prelude to classical version of BhPr. Occlusion of the external ear canals during humming with shanmukhi mudra, another unique feature of BhPr enhances the effect of humming. Research on this variation of BhPr has been growing expeditiously. The acoustics and its overt features can be observed and measured in laboratory conditions which is not common in yoga studies. From various studies done till now it is evident that BhPr influences multiple systems in the body inclusive of the respiratory system. Expression of NO and its role as a therapeutic tool for regulation of respiratory system has been implicated in some BhPr studies that is discussed later in this review.

The classical version of BhPr as in the ancient text, Hatha Yoga Pradipika, includes humming during inhalation also, producing a reverberating sound in high pitch depicting a male bee along with humming during exhalation in a sustained low pitch depicting a female bumble bee. Breathing a physiological process, completes a respiratory cycle with both inhalation and exhalation. It can be observed that the dimension of the acoustics differs from humming during exhalation to humming during inhalation. Experiments made till now have expounded the techniques and efficacy of humming during exhalation and suggest that there is an enhanced expression of NO in the upper respiratory airways⁽²⁾. But to the best of our knowledge, humming during inhalation is an unknown and unexplored domain in scientific research in the context of NO. In this perspective, encouraged by the extraordinary effect of humming during exhalation in enhancing the expression of NO, we hypothesize that humming during inhalation as indicated in classical BhPr may provide efficacious delivery of NO to the required regions of the airways and aid in the optimal level of regulation and maintenance of the lower respiratory and related functions. Classical BhPr may provide a wholesome approach to make optimal use of the crucial molecule NO and derive its benefits to a greater extent.

2 Methodology

In this review we have made an effort to understand the experiments related to the acoustics of humming in enhancing the expression of NO in the paranasal sinuses. It is done with a brief description of NO in general and role of NO in the respiratory airways in particular. A comparison of humming and preliminary version of BhPr is made with the help of yoga texts, scientific literature pertaining to acoustics of humming with reference to literature pertaining to the voice production. A trail is made to evaluate the suitability of BhPr with specific reference to the acoustics in this context. We also examine relevant literature pertaining to the classical version of BhPr which emphasizes on the acoustics of humming both during inhalation and exhalation according to the yoga texts and experiments in the literature pertaining to voice production. We hypothesize that the classical version of BhPr may be a wholesome approach towards enhanced stimulation of NO and provide its effective delivery, to the

lower airways thereby help in its maintenance.

3 Results and Discussion

3.1 Brief Background of Nitric Oxide

NO is a colorless, odourless, hydrophobic, gaseous molecule that has been recognized as an extremely important molecule in biophysics. It has a half-life of 3-5 seconds that diffuses easily through cell membranes. It is a free radical characterized by the presence of an unpaired electron and reacts with several biological compounds which explain its diverse biological effects. NO is produced by various cells throughout the body. It is synthesized by specific enzymes, semi-essential amino acid L-arginine, molecular oxygen, and various Nitric Oxide synthase (NOS) enzymes. The synthase NO has two forms: a constitutive form and an inducible form. The endothelial NOS (eNOS, NOS-I) and neuronal NOS (nNOS, NOS-III), are the two constitutive forms of NO. These eNOS and nNOS are calcium-calmodulin dependent and are activated rapidly and transiently in response to a calcium signal. They are produced in small amounts and provide a rapid pulse-like signal. The functions of endothelial NOS and neuronal NOS are regulated by two distinct types of constitutive NO synthases that have been fully characterized and are widely distributed in the body.

The expression of NO (eNOS) in the endothelial cells is the most important vasodilator mechanism responsible for the maintenance of proper vasomotor function. It is expressed by endothelial cell lining in response to agonists or shear stress. Its physiological role ranges from many other cells and tissue functions, especially in the respiratory, nervous, and immune systems. It promotes the proliferation of smooth muscle cells, platelet aggregation, white blood cell adhesion, and inflammation thereby initiating and aggravating the vascular disease. In patients exposed to vascular risk factors, impaired endothelium-dependent relaxations caused by aging, smoking, diabetes, hypercholesterolemia, hypertension, and sedentary lifestyle are detectable even before any morphological changes could be perceived in the blood vessel wall.

NO (nNOS) is readily expressed through the central nervous system. It has a role in the neural control of cerebral circulation. nNOS is also expressed in peripheral autonomic nerves which modulate blood vessel tone. When over expressed, NO is neurotoxic, and while dysfunctional nNOS signalling has been implicated in cerebrovascular disease states such as ischemia, and migraine, as well as neurodegenerative conditions such as Alzheimer's disease and Parkinson's disease. In cerebral circulation, maintenance of endothelial NO is a crucial strategy in the prevention of cerebrovascular disease and stroke. Endothelial dysfunction in the cerebral circulation may contribute to neurologic diseases.

A third isoform, inducible NOS (iNOS, NOS-II) is not expressed in resting cells but is expressed under pathological conditions as an immune response mediator in white blood cells, epithelial cells, and other cells in response to proinflammatory cytokines. This isoform of NOS is calcium-calmodulin independent, and NO synthesis is transcriptionally controlled and steroid-sensitive. Once the enzyme is activated, it will produce large amounts of NO for a prolonged period and in high concentrations. NO (iNOS) and its reaction products are cytotoxic to viruses, bacteria, tumour cells, and at the same time possibly to host cells too. Whether the upregulated iNOS during inflammation is beneficial or harmful to the host has been debated. Inhibiting iNOS may be considered in the treatment of inflammatory diseases⁽³⁾.

3.2 Nitric Oxide in Paranasal Sinuses

In 1991, NO was detected in exhaled breath in the human breath analysis. The exhaled NO levels exhibited increased levels in asthmatic patients. These observations prompted further research on NO in the respiratory system. Upper airways were found to be the main origin of respiratory NO in healthy adults. This review pertains to NOS in the respiratory airways and its role in the respiratory system. NO concentration in the lower airways is reported to be 20 times lower than in the upper airways in normal subjects.

The para sinuses in the upper airways were found to be the main production site of NO synthesis. It yields very high concentrations, (3000-25000 ppb) with an only minor contribution from the lower airways and oral cavity in healthy subjects. Interestingly, all three isoforms of NOS are available in the upper respiratory tract. eNOS and nNOS are expressed in parasympathetic neurons innervating nasal vessels, endothelial cells, and ciliated epithelial cells. The NOS found in the paranasal sinuses is predominantly calcium-independent, a characteristic usually attributed to the NOS-II, but studies showed that it is constitutively expressed and not inhibited by steroids, the latter being typical features of constitutive NOS. Interestingly, the high expression of NOS-II was found in healthy sinus epithelium. NO, a calcium-independent inducible NOS was found in the epithelial cells lining the sinuses of healthy subjects. Strong NOS immunoreactivity was found apically in those cells in the range of 25 ppm, the highest permissible atmospheric pollution levels for NO. It was surprising at that time to find NOS-II in healthy tissue as it was believed till then that this enzyme was only expressed in inflamed tissues or activated in white blood cells.

This form of NOS is produced continuously in large quantities in the normal sinus epithelial cells, as indicated by the presence of this gas in nasally derived air. NO has been involved in several functions in both the upper and lower airways. NO maintains the physiological homeostasis and regulates the airway inflammation through the expression of three NOS isoforms. NO may also regulate the nasal airway resistance to airflow (NAR). It also seems to humidify and warm the inhaled nasal airflow⁽⁴⁾.

3.3 NO in Sinus Host Defense

From the immuno-histochemical studies, it is noted that iNOS is constantly expressed apically in the paranasal sinus epithelium. This is the enzyme that is used by the white blood cells to produce NO in defense of invasion of viruses, bacteria, or fungi and helps to keep the sinuses sterile. NO could also act as a defense mechanism in the upper airways by modulating the ciliary motility and low levels of NO can be linked to weakened mucociliary activity⁽⁵⁾. Numerous bacteria and many airway pathogens are sensitive to NO gas in concentrations as low as 100 ppb⁽⁶⁾, and the level of NO in the healthy maxillary sinuses is much higher than this. Nasal NO levels are generally very low in patients suffering from sinusitis of different etiology. Primary ciliary dyskinesia (PCD), chronic rhinosinusitis (CRS), and cystic fibrosis are prominent examples of such disorders, characterized by susceptibility to sinus infections and NO release in the nasal airways is virtually absent. However, if the reduced sinus NO is a cause or consequence of sinusitis in these disorders remains to be clarified. It is speculated that lack of NO would decrease the resistance to sinus infections. Altogether it is suggested that NO is involved in sinus host defense to keep them sterile under normal conditions.

3.4 NO as an Aerocrine Messenger

Research over the past few years has shown that NO produced in the paranasal sinuses has a dual function. The high local concentration of NO in the sinuses may act as host defense and contribute to maintaining the sterility of the nasal cavities⁽⁷⁾. Part of the gas leaked to the nasal cavity is diluted in the inhaled breath and is transported by the airstream to the lungs. It is tempting to conjecture that the production of NO in the paranasal sinuses has the purpose of modulating lung function in humans which reduces pulmonary vascular resistance and thus the workload of the heart⁽⁶⁾. NO inhaled from a proximal source will affect pulmonary vessels in contact with ventilated alveoli, thereby improving ventilation/perfusion matching and also reducing vascular resistance. This physiological effect of NO has been termed “aerocrine mediator” to elucidate the airborne transport of the biological messenger connecting the upper and the lower airways in the respiratory tract and providing pulmonary ventilation. Major volume of NO that is produced in the para nasals is transported to the lower airways during normal breathing in a diluted form as low as 10-100 ppb which is observed to reduce pulmonary vascular resistance and facilitate alveolar oxygen transfer into the bloodstream. The volume of the release of NO and transportation through auto inhalation to the lower airways may vary with the volume of breath intake due to various reasons such as airway disease, shallow breathing, wrong postures, and stress. Reduced NO can also lead to disorders in the sinuses as well as the lower airways.

3.5 Paranasal Sinuses, Humming, and Nitric Oxide

Studies by Maniscalco et al. reported that basal NO levels in healthy subjects increase significantly during humming compared to silent exhalation. The paranasal sinuses, notably the maxillary sinus, are an important source of NO. Their research revealed that humming increases NO output 15 folds more than quiet exhalation⁽⁸⁾. This is caused by humming-induced air oscillation which increases air exchange between the paranasal sinuses and the nasal cavity. The paranasal sinuses occur in four pairs, hollow, air-filled cavities located on either side of the nose in the skull bone. Importantly, the epithelium of the maxillary sinuses located in the skull just below the eyes contains an enzyme that produces large amounts of NO. The paranasal sinuses form a compartmentalized reservoir of NO. They communicate through small outlets known as ostia, through which fluids and gases pass in both directions. Several studies in recent times offer many crucial and interesting findings. It is observed that the volume of the sinus cavities and their connectivity via the sinus ostia to the nasal cavity renders them acoustically Helmholtz resonators with the neck corresponding to the ostia. The sinusoidal alternating acoustic pressure due to humming, forces the air plug in the Helmholtz resonator neck (ostium of the paranasal sinus) to vibrate, consequently expelling NO from the paranasal sinuses to the nasal cavity. Experiments have revealed that this evacuation varies with the frequency. The resonance between Helmholtz frequency and frequency of the humming is one of the important factors contributing to a higher volume of NO evacuation. Maintaining the sustained frequency of humming is said to contribute to achieving the Helmholtz resonance frequency. The release of NO peaks when the humming sound is produced at the narrow range of fundamental frequency of the voice (both males and females). The average fundamental frequency of the vocal folds during voice production is in the range of 100-150 Hz for males and 180-250 Hz for females. Another factor that contributes to the evacuation of NO is the size of the ostia. The acoustic component of breath during humming seems to rapidly wash out NO from the sinuses. The endothelial cells of the

sinuses can replenish the depleted levels of NO when there is a gap of just three minutes between two humming sessions⁽⁹⁾.

It is also to be noted that research carried out till now pertains to humming during the exhalation phase of breathing or exhalation phonation. It has been demonstrated that the techniques of exhalation phonation may enhance the expression of NO.

3.6 Humming vs *Bhramari Pranayama*

Humming has been part of the ancient technique of yogic breathing, *Bhramari Pranayama* (BhPr). It is classified as swara pranayama as it includes the dimension of acoustics in breath regulation. BhPr is generally practiced by humming during exhalation in a sustained low pitch emulating a female bee. Generally, in BhPr, humming is produced during exhalation preceded by controlled inhalation. Humming is performed using one of the nasal consonants [m], [n], or [ŋ]. These nasal consonants, when hummed are said to produce maximum resonance. Humming is performed at a sustained low pitch to emulate the buzz of a female bee which coincides with the fundamental frequency of human voice production across genders⁽¹⁰⁾.

Occluding the external ear canal with middle fingers or by applying shanmukhi mudra is another important feature of BhPr. This mudra is carried out using all the fingers; thumbs of both hands to occlude the two ear canals, forefingers to place on the closed upper eyelids, the middle fingers on the nasal bridge to perceive the facial vibration and to partially block and regulate the passage of the breath and lastly, the ring, and the little fingers to be placed on the upper and lower lips⁽¹¹⁾. Occluding ear canals enhance the perceived loudness of acoustic vibrations of the self-produced humming⁽¹²⁾.

According to the classical variation in the ancient text, Hatha Yoga Pradipika, BhPr is performed by humming during both inhalation and exhalation; a quick inhalation, making a reverberating sound like a male black bee, and slow exhalation while softly making the sound of a female black bee in a low pitch along with shanmukhi mudra. It is also classified as one of the ashta kumbhakas (eight pranayamas with breath retention). It is classified as a kumbhaka, as breath retention between inhalation and exhalation is performed.

Literature about speech/voice production has termed humming during exhalation as exhalation phonation and humming during inhalation as inhalation phonation. Both types of humming are used for therapeutic purposes in voice production. During phonation, the vocal folds come sufficiently close, which increases trans-glottal pressure causing the vocal folds to vibrate thereby creating a modulated airflow. It is also observed that the vibratory cycle of the vocal folds during inhalation phonation is a reversal of exhalation phonation. During exhalation phonation, breath flows upwards from the lungs and moves towards the nasal and oral cavities. During inhalation phonation, breath flows towards the lungs from the upper airway. Literature about voice production report that the natural pitch of humming during inhalation is higher than the humming during exhalation due to the lengthening and thinning of vocal folds. The acoustic component of humming during inhalation is said to be less sonorous and harsher sounding and has lesser clarity than the exhalation humming. Manipulation of the sinus and/or oral/pharyngeal cavities during inhalation phonation increases resonance than during the exhalation phonation⁽¹³⁾. Studies have noted that the fundamental frequency of the inhalation phonation is higher than the exhalation phonation on an average of 5.1 semitones; for men, the increase is from 101 Hz to 133 Hz and for women, 202 Hz to 289 Hz. An increase of more than 50% airflow during inhalation phonation than the exhalation phonation is also observed in these experiments⁽¹⁴⁾.

It is also postulated that nasal Nitric Oxide output is considerably greater during inhalation than exhalation in healthy adults⁽⁶⁾. The ostial opening of the sinuses which oscillate to acoustic vibration is said to respond to humming during inhalation similar to humming during exhalation as already observed in various experiments⁽¹⁵⁾. Humming during inhalation is observed to facilitate effective transportation of NO produced to the lower airways. A general widening of the supraglottis and the larynx assuming a lower neck position during inhalation phonation is observed, perhaps to facilitate the increased airflow into the lungs. This denotes that the increased pressure, volume, and intensity of the sound may cause a higher volume of airflow into the lungs thereby increasing the volume of NO. It is opined that the inhalation maneuver creates a negative pressure in the sinuses thereby forcing NO-containing gas out of the cavities into the posterior oropharynx and effectively transported to the lungs. The supply of gases between the nose and sinuses to the lungs, during inhalation and exhalation, is said to be powered by an efficient aerodynamic system⁽¹⁶⁾.

The above information seems to support that the features of classical BhPr during inhalation may aid in better utilization of NO in the airways of the respiratory system. But to the best of our knowledge, research pertaining to humming during inhalation in the context of NO is yet to be done. Experiments with alternate exhalation humming and inhalation humming are also essential. As the exhalation part of BhPr is very encouraging, the corresponding inhalation part may also yield a similar outcome and aid in the better utility of NO to enhance health benefits.

Humming is an exceptional mechanism when volitionally performed in a certain way as reported by various studies, can stimulate a many-fold increase in NO production than during quiet exhalation. Humming enhances the NO concentrations in the para sinuses from the range of up to 20 ppm to the range of 200 ppm or more which is known to serve as anti-fungal

also. Higher concentration of NO aids in better maintenance of para sinuses, which is critical to supply continuous NO to the lower airways of the respiratory system. The increased level of NO seems to be useful to treat nasal ailments such as chronic rhinosinusitis (CRS) caused by immune disorder by fungi. However, the role of an excessive amount of NO produced in inflammation which remains elusive is to be carefully examined in this context.

A case reported by Eby, George A. of a subject with chronic rhinosinusitis treated with antirhinoviral, antiherpetic, and oral antibiotics and oral decongestants was ineffective. He was administered humming at a low pitch, 60-120 times in four sessions per day for four days. As a result, all rhinosinusitis symptoms were essentially eliminated within four days⁽¹⁷⁾. Interestingly BhPr also seem to have a similar effect on chronic rhinosinusitis. (CRS) A randomized controlled study of CRS was conducted, with BhPr as intervention. The study recruited 60 patients who were randomly divided into two groups, one received conventional treatment, and the other group was given to practice BhPr humming during exhalation. The patients were advised to practice BhPr twice a day and were followed up at 1, 4, and 12 weeks using the Sino-Nasal Outcome Test (SNOT-22 score). The results were analysed and the individual SNOT-22 scores at 1st, 4th, and 12th weeks were compared with the baseline SNOT scores. There was a statistically significant improvement in scores by the 4th week ($p=0.0008$) and it continued until the 12th week ($p<0.00001$)⁽¹⁸⁾. Apart from chronic rhinosinusitis, (CRS) BhPr was also found to be effective in improving the pulmonary function of the chronic obstructive lung disease (COPD) patients. In a study done on COPD patients, with BhPr as an intervention for 12 weeks, a significant reduction in dyspnoea among the patients was observed⁽¹⁹⁾. It is also hypothesized that, BhPr prevents coagulopathies and morbidity due to Covid-19, by enhancing the expression of NO and increased carbon dioxide by extended exhalation along with alkaline pH⁽⁸⁾.

Nitric Oxide is an important biomarker in exhaled breath, as it is investigated in various pulmonary and non-pulmonary diseases. Measurement of NO in exhaled breath is used as a clinical tool to measure airway inflammatory diseases including asthma. The nasal NO was observed to be lower in ailments such as primary ciliary dyskinesia (PCD) and cystic fibrosis (CF) due to obstruction of the paranasal sinuses. In these ailments measuring exhaled NO during humming is recommended as it increases the sensitivity of the blocked condition of the ostiomeatal complex⁽²⁰⁾.

Scientific research on acoustics of humming in the context of expression of NO in the para sinuses has made it possible to understand the efficacy of this technique to a great extent. It is also observed that the existing anatomy of the para nasals, maxillary sinuses, in particular, operate as Helmholtz resonators. These structures would resonate, when hummed at the fundamental frequency of voice at constant pressure, , due to which production of NO would be at peak level. Typically, humming per se does not define the pitch or the consistency of the pitch that is to be maintained. However, BhPr specifically indicates the pitch of the humming, and the consistency of the pitch to be maintained. These specifications seem to match with the observations made in the experiments of humming during exhalation that have proven to produce the highest level of NO. Based on these observations we argue that BhPr could be a better option in comparison to humming to efficient increase of expression of NO in the paranasal sinuses.

Another limitation of humming is that, it does not seem to provide for efficient delivery of additional NO released by humming to the lower airways. It is postulated that the prime purpose of expression of NO in the para nasals sinuses is to provide NO through auto inhalation to regulate pulmonary functions. It is also suggested that due to short lifetime of a few seconds to NO and diffusion distance, increased endogenous NO supply at low-dosage may be necessary to improve pulmonary effect in the lungs⁽²¹⁾. Optimal supply of NO is also necessary to maintain ventilation to perfusion ratio matching, decrease pulmonary vascular resistance and thereby decrease the workload of the heart. Depletion of NO availability is known to adversely affect the these functions and also immunity of the airways leading to various diseases and infections.

In recent clinical trials, to overcome the depletion of physiological inhaled endogenous NO and treat consequent ailments, exogenous NO is resorted to. The exogenous NO is administered via mechanical drug delivery systems, many systems with include acoustics, are used extensively. This Inhaled Nitric Oxide is utilized to manage pulmonary arterial hypertension and ventilation-perfusion mismatch associated with cardiac pulmonary ailments. However extensive use of inhaled exogenous NO is limited by logistical and financial barriers. Observations made in the experiments of acoustics of humming during exhalation may help in understanding better management of drug delivery system.

We hypothesize that humming during inhalation may supply optimal quantity of NO to the upper and lower airways of the respiratory system. Humming during inhalation may efficiently supply NO to the sinuses to treat upper airway diseases. Regular practice of BhPr may help to strengthen the respiratory system and can be a preventive measure to many ailments. In classical version of BhPr, both exhalation and inhalation humming are alternatively done to complete a breathing cycle. Breath is held in-between inhalation and exhalation. In pranayama techniques according to the yogic texts, holding the breath in-between inhalation and exhalation is said to be very effective. Holding breath after inhalation may give enough time for gas exchange in the lungs and improve ventilation/perfusion ratio matching. Further, holding the breath after exhalation may provide time for the paranasal sinuses to replenish NO after evacuation. We need further experiments to understand this phenomenon and its

application for clinical purposes.

The technique of classical BhPr, adding the dimension of specific acoustics to both inhalation and exhalation with appropriate breath-holding in-between may tremendously enhance the expression of NO and cater to its effective end use. This may help to maintain and efficiently regulate the respiratory system; it may also strengthen the respiratory system to boost its overall efficacy.

4 Conclusion

Inhalation of endogenous NO expressed in the upper airways of the respiratory system, can markedly affect a wide range of processes related to the physiology and pathology. The respiratory airways are provided with the paranasal sinuses that has a significant biological role of producing the major part of NO. NO is involved in regulation of many crucial functions like being the host defense and regulation of pulmonary functions. Experiments have shown that implementing the humming during exhalation and simple yogic concepts of BhPr, offers a unique opportunity to enhance the capacity of the existing anatomical structure in endogenous generation of additional NO. We propose that the other part of classical BhPr i.e., humming during inhalation as defined by the yogic texts may also offer similar results. Understanding the relevance of physical aspects like frequency, resonance and geometry of the paranasal sinuses for NO release in enhancing the prime purpose of the physiological functioning seem to make an enormous difference. This calls for additional studies as it is expected that further advances in this direction may ameliorate the role of NO in fine tuning the regulatory functions, measurement methods, drug delivery systems. Advances in this direction may pave way to development of diagnostic, therapeutic and monitoring processes of several critical respiratory diseases and perhaps help in promoting better health.

References

- 1) Ignarro LJ. Nitric oxide is not just blowing in the wind. *British Journal of Pharmacology*. 2019;176(2):131–134. Available from: <https://doi.org/10.1111/bph.14540>.
- 2) Ambrosino P, Molino A, Spedicato GA, Parrella P, Formisano R, Motta A, et al. Nasal Nitric Oxide in Chronic Rhinosinusitis with or without Nasal Polyps: A Systematic Review with Meta-Analysis. *Journal of Clinical Medicine*. 2020;9(1):200. Available from: <https://doi.org/10.3390/jcm9010200>.
- 3) Zhu HY, Hong FF, Yang SL. The Roles of Nitric Oxide Synthase/Nitric Oxide Pathway in the Pathology of Vascular Dementia and Related Therapeutic Approaches. *International Journal of Molecular Sciences*. 2021;22(9):4540. Available from: <https://doi.org/10.3390/ijms22094540>.
- 4) Trivedi GY, Saboo B. Bhrumari Pranayama – A simple lifestyle intervention to reduce heart rate, enhance the lung function and immunity. *Journal of Ayurveda and Integrative Medicine*. 2021;12(3):562–564. Available from: <https://doi.org/10.1016/j.jaim.2021.07.004>.
- 5) Shapiro AJ, Dell SD, Gaston B, O'Connor M, Marozkina N, Manion M, et al. Nasal Nitric Oxide Measurement in Primary Ciliary Dyskinesia. A Technical Paper on Standardized Testing Protocols. *Annals of the American Thoracic Society*. 2020;17(2):1–12. Available from: <https://doi.org/10.1513/AnnalsATS.201904-347OT>.
- 6) Bazak R, Elwany S, Mina A, Donia M. Nitric oxide unravels the enigmatic function of the paranasal sinuses: a review of literature. *The Egyptian Journal of Otolaryngology*. 2020;36(1). Available from: <https://doi.org/10.1186/s43163-020-00011-7>.
- 7) Nair G, Nandhan R, Otolaryngol MK. 2020. Available from: <https://www.researchgate.net/profile/Raghu-Nandhan/publication/343237144>.
- 8) Taneja MK. Modified Bhrumari Pranayama in Covid 19 Infection. *Indian Journal of Otolaryngology and Head & Neck Surgery*. 2020;72(3):395–397. Available from: <https://doi.org/10.1007/s12070-020-01883-0>.
- 9) Granqvist S, Sundberg J, Lundberg JO, Weitzberg E. Paranasal sinus ventilation by humming. *The Journal of the Acoustical Society of America*. 2006;119(5):2611–2617. Available from: <https://doi.org/10.1121/1.2188887>.
- 10) Ushamohan BP, Belur YK, Rajasekaran AK, Ilavarasu J, Srinivasan TM. A Framework of Measurable Features of Bhrumari Pranayama Leading to Meditation. *Indian Journal Of Science And Technology*. 2023;16(4):259–265. Available from: <https://doi.org/10.17485/IJST/v16i4.752>.
- 11) Ushamohan BP, Rajasekaran AK, Belur YK, Srinivasan TM, Ij. Bhrumari Pranayama as an aid to meditation : A review of classical yoga texts. *Int J Yoga-Philosophy*. 2020;1(8):58–68. Available from: https://doi.org/10.4103/ijny.ijoyppp_21_19.
- 12) Howell P, Williams M, Dix H. Assessment of Sound in the Ear Canal Caused by Movement of the Jaw Relative to the Skull. *Scandinavian Audiology*. 1988;17(2):93–98. Available from: <https://doi.org/10.3109/01050398809070697>.
- 13) Deboer A. Ingressive phonation in contemporary vocal music. 2012. Available from: http://rave.ohiolink.edu/etdc/view?acc_num=bgsu1353356284.
- 14) Orlikoff RF, Baken RJ, Kraus DH. Acoustic and physiologic characteristics of inspiratory phonation. *The Journal of the Acoustical Society of America*. 1997;102(3):1838–1845. Available from: <https://doi.org/10.1121/1.420090>.
- 15) Jankowski R, Nguyen DT, Poussel M, Chenuel B, Gallet P, Rumeau C, et al. 2016. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S187972961630093X>.
- 16) Gungor AA. The aerodynamics of the sinonasal interface: the nose takes wing-a paradigm shift for our time. *International Forum of Allergy and Rhinology*. 2013;3(4):299–306. Available from: <https://doi.org/10.1002/alf.21105>.
- 17) Andhavarapu A, Dhopathi SR. Yogic-humming: A Respiratory Defense Booster for COVID Times. *The Journal of Contemporary Dental Practice*. 2021;22(7):721–723. Available from: <https://doi.org/10.5005/jp-journals-10024-3134>.
- 18) Abishek K, Bakshi S, Bhavanani A. The efficacy of yogic breathing exercise Bhrumari pranayama in relieving symptoms of chronic rhinosinusitis. *International Journal of Yoga*. 2019;12(2):120. Available from: https://doi.org/10.4103/ijoy.IJOY_32_18.
- 19) Jayasheela H. Efficacy of Bhrumari Pranayama on Dyspnoea among the Patients with Chronic Obstructive Pulmonary Disease. 2021.
- 20) Maniscalco M, Pelaia G, Sofia M. Exhaled nasal nitric oxide during humming: potential clinical tool in sinonasal disease? *Biomarkers in Medicine*. 2013;7(2):261–266. Available from: <https://doi.org/10.2217/bmm.13.11>.

- 21) Alimoradi H, Greish K, Gamble AB, Giles GI. Controlled Delivery of Nitric Oxide for Cancer Therapy. *Pharmaceutical Nanotechnology*. 2019;7(4):279–303. Available from: <https://doi.org/10.2174/2211738507666190429111306>.