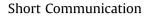
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Nasal application of sesame oil-based *Anu taila* as 'biological mask' for respiratory health during COVID-19



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ABSTRACT

This article narrates the potential role of sesame oil-based *Anu taila* for respiratory health and the prevention of COVID-19. Ayurveda recommends the use of sesame oil and *A. taila* as a part of daily routine (dinacharya) for oral gargling and transnasal application (*Nasya*) for preventing upper respiratory tract infections. Recent studies on COVID-19 have elucidated the activity of certain fatty acids in restricting viral binding. Based on the evidence gathered from in-silico, pre-clinical, and pharmacological studies as well as references from classical textbooks of Ayurveda, this article infers that the transnasal application of sesame oil and/or *A. taila* could provide resilience/protection to the respiratory system. It can act as a 'biological mask' to prevent respiratory infections like COVID-19. Detailed pharmacological study can give fuller confirmation of our informed "inference" that *A. taila* offers a cost-effective intervention for the prevention of COVID-19 like infections of the upper respiratory tract.

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1. Background

Since the outbreak of SARS-CoV-2, the cases of respiratory infections skyrocketed causing 278 million incidents and 5.4 million deaths globally between 2019 and 2021 [1]. The discovery of vaccines has resulted in a significant reduction in mortality [2,3]. However, despite the vaccine's efficacy, the re-emergence of resistant strains and breakthrough infections makes prevention quite challenging [4–6]. In India, the rate of breakthrough COVID-19 infections in fully vaccinated individuals was reported to be 4-6% [7,8]. Hence, long-term general and efficient respiratory preventive solutions even beyond the current pandemic are a public health priority.

Recent research has looked at the use of fatty acids for possible antiviral effects against COVID-19 [9–11]. Omega-3 fatty acids such as alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and its derivatives were used in several viral proteins [14–16]. During SARS-CoV-2, a study performed at the start of 2020 attempted to investigate the activity of natural product compounds against the viral proteins. It was seen that the interaction between phytoestrogens (like Diadiazin, Genistein, Formontein, and Biochanin-A) and fatty acids (like palmitic acid, linoleic acid, and chlorogenic acids) with host viral recognition site SBD β resulted in antagonistic activity against viral binding [17]. Following this, Toezler et al., performed a noteworthy in-silico molecular docking study of an essential fatty acid, linoleic acid against viral proteins [18]. Computational analysis showed that linoleic acid exhibited excellent and strong interaction at all the 3 binding sites of the SARS-CoV-2 spike proteins. Toezler et al. further verified the intensity of Spike protein-ACE2 binding in an in-vitro model. An interaction with linoleic acid caused a conformational change in the viral protein to a locked S structure that reduced the affinity of binding with host ACE2 receptors. It was also seen that no mutations of the viral genome resulted in any changes in the binding site for linoleic acid. Further, when epithelial cells infected

inflammation-associated chronic respiratory diseases [12,13]. Similar exploration was done during the SARS, MERS and other

viral infections, elucidating the mechanism of fatty acid-binding to

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with SARS-COV-2 were treated using various doses of remdesivir, the presence of linoleic acid provided a synergistic action in antiviral activity despite the dosage. Therefore, a low dose of Remdesivir was sufficient in treating infection in presence of linoleic acid [18]. Subsequent to this, another group investigated the interaction of spike proteins with 17 polyunsaturated free fatty acids (PUFA). From the docking, PUFAs like linoleic acid, eicosapentaenoic acid. and linolenic acid interfered with ACE2 receptors of the virus significantly, preventing its binding to the host ACE2 receptors. Similar to the outcomes by Toezler et al., linoleic acid among others showed excellent inhibition in the binding of the RBD sequence of SARS-CoV-2 with ACE2 receptors. Interestingly, two other PUFAs, linolenic acid, and eicosapentaenoic acid also reduced the activity of host proteases (TMPRSS2 and cathepsin L) that activate spike proteins, thus reducing the affinity of binding with ACE2 receptors and inhibiting the viral entry [19]. Several studies on SARS-CoV-2 have also shown similar involvement of fatty acids as potent antivirals for SARS-CoV-2 [20-22]. These studies indicate the ability of essential fatty acids, especially linoleic acid, as a notable compound inhibiting viral binding and interactions. An electron micrograph on linoleic acid has also shown that a concentration of 1 mg/ml of linoleic acid is capable of completely disrupting the viral envelope, inactivating the viral activity [23].

Few studies have accessed the fatty acids from whole oils too. In a computational analysis on the activity of sesame oil and its compounds against the SARS-CoV-2 viral proteins, 6 compounds from the oil had higher affinity compared to the currently used Mpro inhibitor, darunavir, against viral M-pro, and an equivalent docking score compared to the standard drug, remdesivir in RdRp binding [24]. A similar study on seed proteins including sesame oil reported key molecules of sesame (Sesamin, sesaminol, sesamolin) having significantly good interaction with 3 important viral proteins (spike protein, M-pro, and ACE receptor site) [25]. Likewise, in a study conducted on all the fatty acids of coconut oil against viral proteins [26], fatty acids like capric acid, caprylic acid, lauric acid, linoleic acid, myristic acid, oleic acid, palmitic acid, and oleic acid exhibited good inhibition against 6 proteins of SARS-CoV-2 in binding to the host receptors. Surprisingly, despite the abundance of lauric acid (44%) in coconut oil, a stronger affinity was seen with linoleic acid(1%) against 5 of the 6 SARS-CoV-2 protein targets [26]. Interestingly, sesame oil consists of about 41-48% linoleic acid and is the most abundant fatty acid seen in sesame oil in addition to other fatty acids like oleic acid (35-42%), palmitic acid (7-9%), and stearic acid (4-5%) [27].

2. Anu taila for respiratory health

Independent of these scientific explorations of oils against infections that began only in the late 20th century, Ayurveda has based on its theoretical framework (*Dosha Vichar*) practiced the use of oils for prevention and protection against the entry of external agents for centuries [28]. Some commonly used oils for nasopharyngeal protection include Sesame oil, Coconut oil, and Castor oil [29]. Of these, sesame oil (*Tila taila*), extracted from the plant *Sesamum indicum, Linn,* known as "queen of oil seeds" is given paramount importance in nasopharyngeal and other medicinal applications [30–32]. Application of pure sesame oil trans-nasally improved linings of nasal mucosa preventing mucosal dryness [33], attenuating edema and neutrophilic inflammation in lungs [34], and offering protection of the upper respiratory tract [35]. The presence of PUFAs, and phytochemicals makes sesame a rich source of antioxidants, with longer stability, high resistance to oxidation, and rancidity [36]. Its application as antioxidant, anti-carcinogenic, analgesic, anti-bacterial, and anti-inflammatory agent are also well-known [37–39].

For respiratory health, as prophylaxis, Ayurveda specifically advocates the use of sesame oil-based medicated oils like A. taila (sesame oil infused with 25 other herbs) and Murchitatila taila (sesame oil infused with herbs and processed by a method called 'Murchana') as transnasal and oral lubricants [40]. Particularly. A. taila is recommended in classical texts to be used as part of dinacharya (daily regimen) for transnasal application (Nasya) [40,41]. It is said to strengthen all the sense organs and is used for diseases above the clavicle (urdwajatrugata: urdwa-above, Jatruclavicle) including upper respiratory diseases [40]. The method of preparation A. taila includes a technique called Murchana will be seen as an extremely innovative process by technologists. The oil is repeatedly boiled with the herbal decoction (of more than 25 herbs) 9 times and during the 10th time, goats' milk is added to the mixture. A study investigated the physicochemical changes in oils after the process of 'murchana'. It was seen that murchana oils prepared as per ayurvedic classical method showed higher saponification, refractive index, decreased iodine, free fatty acids, and peroxide levels and dramatically improve the stability i.e., reduce the onset of rancidity, compared to unprocessed oils. The Murchana process increased the bioavailability of low molecular weight fatty acids, thus facilitating easy absorption by the body [42]. When the classical method of oil preparation was replaced with a deviated method of preparation, an increased peroxide level was seen [43]. Whereas, the classical form of preparation showed better dissolution of herbal components, an unaltered fatty acid profile of sesame oil, and high intensity of herbal components [43]. These experiments highlight the Ayurvedic system's keen use of advanced processing methods for enhanced functionality of medicated sesame oil, A. taila. Furthermore, Duraipandi et al. [44] identified that the active polar botanical ingredients (ABIs) of A. taila were found embedded in a network of vesicular structures of the lipid base to form a nano-drug delivery system. Thus efficiently delivering water-soluble ingredients across barriers [44].

During the outbreak of SARS-CoV-2, Ministry of AYUSH, Govt. of India, guidelines also recommended the use of sesame oil or A. taila for transnasal application and oral swishing as a preventive guideline [32]. An insightful study showed that SARS-CoV-2 infected hamsters when treated with either pure sesame oil or A. taila through the transnasal route, there was a significant reduction in the pro-inflammatory cytokines Th1 and Th-17 in both groups. A better reduction in the rate and severity of infection, and pneumonitis symptoms when A. taila was used [43]. Nasal mucosa exhibits the highest ACE2 expression and is the origin of viral transmission [20]. Therefore, the use of sesame oil or A. taila as transnasal usage (Nasya) might avoid the adherence of the virus possibly by forming a biofilm [29,30]. Though studies on A. taila are limited, we can speculate from the above studies that medicated A. taila has significantly better activity than pure sesame oil in respiratory health. It will be an intriguing exploration to determine the activity and composition of all the fatty acids from sesame oil and A. taila against SARS-CoV-2.

3. Chemical profiling of sesame oil, *Anu taila* and *Murchitatila taila*

The authors of this paper conducted a pilot experiment to determine the fatty acid compositional profile of pure sesame oil, *A. taila*, and *Murchitatila taila* using Gas Chromatography (GC)

(Shimadzu), RT 2560 column (100 m, 0.25 mm id, 0.20 µm df, 250 °C max temperature) with Helium as carrier gas (flow rate 1 ml/min). We detected high amounts of oleic and linoleic acid (polyunsaturated essential fatty acid) in addition to significant levels of palmitic acid and stearic acid from pure sesame oil. *Murchitatila taila*. prepared using sesame oil by a special process called 'Murchana' showed little variation in fatty acid composition as compared to native sesame oil primarily in terms of concentration of palmitic and oleic acid. While the amount of linoleic acid was found to have slight increase which can be considered significant. A. taila showed minimal variations in the composition of free fatty acids compared to sesame oil, despite its complex 10 steps preparative process. The presence of additional fatty acids such as medium-chain capric acid, caproic acid, lauric acid, long-chain myristic acid, and lignoceric acid was also seen (Table 1). A. taila along with herbs also consists of goat's milk and traces of coconut oil as its ingredient. Goat's milk is known for its anti-viral effects and its use in the treatment of many chronic respiratory diseases [43]. These additional ingredients presumably be the source of imparting additional fatty acids detected in A. taila which were originally absent in sesame oil. To validate absence of any adulterant in these oils we also compared the fatty the composition with some of market refined and cold pressed sesame oil samples and found the composition to be significantly in alignment with the literature reports [45]. Few studies also report the antiviral properties of goat's milk in COVID-19 [46]. A comparative analysis of fatty acid profile of goat's milk with sesame oil, A. taila and murchita tila taila showed the presence of four fatty acids viz. n-Caproic acid (C6), Capric acid (C10), Lauric acid (C12) and Myristic acid (C14) in both *A. taila* and goat's milk (Table 2). The fatty acid profile of goat's milk was obtained from previous research works [47,48]. Among these, n-Caproic acid (C6), Capric acid (C10) and Lauric acid (C12) were absent in both sesame oil and *murchita tila taila* indicating the importance of adding goat's milk in *A. taila* preparation. Also, the presence of Myristic acid (C14) in *murchitatila taila* indicate that it may be coming from other ingredients as well and further studies are needed to confirm this observation. Similarly, detailed analysis is required to understand the source of fatty acids like cis-13-Octadecenoic acid (C18:1-cis-13), cis-11,14-Eicosadienoic acid 8,11-Octadecadienoic acid and Lignoceric acid (C24) that were found only in *A. taila* and not in sesame oil, *murchitatila taila* and goat's milk.

While this experiment does not validate the application of *A. taila* in SARS-CoV-2, it does signify the retained and enhanced expression of many fatty acids seen in sesame oil, including linoleic acid. Thus, administering *A. taila* could provide better resilience of respiratory health.

From the studies discussed above on fatty acids, we can infer that linoleic acid, abundantly seen in sesame oil, consists of potent antiviral activities against viral binding and infection. Further, recent experimental explorations on sesame oil and *A. taila*, signify the retained, unaltered and enhanced functionality of *A. taila* in respiratory health. We can reasonably infer that the use of sesame oil and *A. taila* as transnasal therapy could play a role of primary protection, and act as a "biological Mask" against SARS-CoV-2 infection and for general protection of the upper respiratory system against various infections.

Table 1

Composition of fatty acids in pure sesame oil, and medicated oils (Anu tail and Murchitatila taila).

FATTY ACID	Pure Sesame Oil		Anu Taila			Murchita tila taila		Market Refined Oil					Market Cold Pressed Oil			Literature Ses. Oils [45]	
	mg/g	%	mg/g	%	mg/g	%	Sam	ple-1	Sam	ple-2	Sam	ple-3	Sam	ple-1	Sam	ple-2	%
n-Caproic acid (C6)			0.49	0.04	-	-			-				-	-			
Capric acid (C10)			0.76	0.08	-	-			-				-	-			
Lauric acid (C12)			1.453	0.15	-	-			-				-	-			
Myristic acid (C14)			5.42	0.54	7.091	0.71			-				-	-			
Palmitic acid (C16)	100.3	10.0	107.0	10.7	220.9	22	85.94	8.59	88.17	8.81	87.64	8.77	81.46	8.14	79.39	7.93	9.3 - 10.15
Palmitoleic acid (Cis-iso) (C16:1)	1.101	0.11	1.804	0.18	5.567	0.55	1.4	0.14	0.93	0.09	0.73	0.07	0.89	0.09	0.826	0.08	0.10 - 0.13
Margaric acid (C17)	0.649	0.06	0.343	0.03	0.964	0.1			0.36	0.04			-	-			
Stearic acid (C18)	69.33	6.92	68.26	6.83	44.16	4.4	58.05	5.81	53.3	5.33	50.02	5	55.02	5.5	55.89	5.58	5.5 - 7
cis-13-Octadecenoic acid, methyl ester (C18: 1-cis-13)			1.71	0.17	-	-			-				_	-		ł	
Oleic acid (C18: 1-cis-9)	427.4	42.6	435.5	43.55	272.4	27.1	402.9	40.2	418.7	41.84	421.9	42.21	428.5	42.81	430.6	43.01	39.8 - 48.8
cis-11,14 Eicosadienoic acid, methyl ester 2. 8,11-Octadecadienoic acid			1.404	0.14	-	-			-				_	-		-	
Methyl 9-cis, 11-trans- octadecadienoate (CLA)			-		-	-	1.89	0.19	-				-	-		ł	
Methyl 10-trana, 12-cis- octadecadienoate (CLA)			-		-	-	1.42	0.14	-				-	-		ł	
Lenoleic acid (C18:2)	388.1	38.76	360.9	36.1	438.3	43.65	431.5	43.16	425.7	42.54	426.9	42.7	421.3	42.09	418.6	41.82	31.8 - 41.7
Arachidic acid (C20)	7.472	0.75	7.988	0.8	4.794	0.48	7.07	0.71	6.82	0.68	6.48	0.65	7.26	0.73	7.233	0.72	
cis-11-Eicosenoic acid (C20:1)	2.215	0.22	1.831	0.18	0.798	0.08	2.26	0.23	1.8	0.18	1.46	0.15	1.09	0.11	1.426	0.14	
Linolenic acid (C18:3)	3.215	0.32	2.767	0.28	1.959	0.2	5.63	0.56	2.48	0.25	2.49	0.25	2.42	0.24	2.07	0.21	0.26 - 0.5
Methyl 20-methyl- heneicosanoate (C23)	1.63	0.16	1.427	0.14	1.941	0.19	1.79	0.18	1.65	0.17	1.15	0.12	1.33	0.13	1.38	0.14	
Methyl 14-methyl- eicosanoate (C22)			-		-	-			-		0.91	0.09	-	-		-	
Lignoceric acid (C24)			0.901	0.09	-	-			-				0.58	0.06	1.12	0.11	
Methyl 22-methyl- tetracosanoate (C26)			-		0.974	0.1			-				-	-		-	

Shaded values are signifying fatty acids present in high concentrations for ex. Palmolive, Stearic, Oleic, Linoleic acids and nutritionally important fatty acids Ex. Linolenic acid: which is an omega-3 fatty acid.

Table 2

Comparative analysis of fatty acid profile of goat's milk with sesame oil, Anu taila and murchita tila taila.

Fatty Acids	% of fatty acid content in								
Fatty Acids	Sesame Oil	Anu Taila	Murchitatila Taila	Goat Milk					
Butyric acid (C4)		-		2.07					
n-Caproic acid (C6)		0.04		1.99					
Caprylic acid (C8)		-		2.28					
Capric acid (C10)		0.08		2.08					
Lauric acid (C12)		0.15		4.1					
Myristic acid (C14)		0.54	0.71	10.54					
Pentadecanoic acid (C15)		-		0.99					
Palmitic acid (C16)	10.02	10.7	22	29.7					
Palmitoleic acid(Cis-iso) (C16:1)	0.11	0.18	0.55	1.09					
Margaric acid/Heptadecanoic acid (C17)	0.06	0.03	0.1	0.69					
Stearic acid (C18)	6.92	6.83	4.4	9.07					
Myristoleic acid (C14:1 (c9))		-		0.29					
cis-13-Octadecenoic acid, methyl ester (C18:1-cis-13)		0.17		-					
Elaidic acid (C18:1- trans-9)/Oleic acid (C18:1-cis-9)/ Petroselinic acid (C18:1- cis-6)	41.62	42.48	26.23	20.52					
Oleic acid (C18:1-cis-9)/ Elaidic acid (C18:1- trans-9)	1.06	1.07	0.9	_					
cis-11,14-Eicosadienoic acid, methyl ester; 8,11-Octadecadienoic acid		0.14		_					
Methyl 9-cis,11-trans-octadecadienoate (c9 t11 C18:2- CLA)		-		0.81					
Methyl 10-trans,12-cis-octadecadienoate (c12 t10 C18:2- CLA)		-		-					
Linoleic acid (C18:2)	38.76	36.1	43.65	2.07					
Arachidic acid (C20)	0.75	0.8	0.48	-					
cis-11-Eicosenoic acid (C20:1)	0.22	0.18	0.08	-					
Linolenic acid (C18:3)	0.32	0.28	0.2	0.35					
Methyl 20-methyl-heneicosanoate (C23)	0.16	0.14	0.19	-					
Methyl 14-methyl-eicosanoate (C22)		-		-					
Lignoceric acid (C24)		0.09		-					
Methyl 22-methyl-tetracosanoate (C26)		_	0.1	-					

The highlighted fatty acids signify common candidates between Goat's milk and Anu Taila presumably indicating that those fatty acids might have been incorporated to Anu Taila from Goat's milk

4. Conclusion

This article intends to inform the public and the scientific world about the safety in use of sesame oil and *A. taila* as transnasal therapies for respiratory health. Furthermore, the article makes an informed inference based on supportive Ayurveda derived as well as scientific evidence that it can serve as a biological mask.

While physical masks and shields should certainly be used for protection, transnasal installation of medicated oils like *A. taila* or pure sesame oil will help in providing additional and effective nasopharyngeal protection. The idea of a biological mask is also a simple and practical measure.

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Conflicts of interest

Prof. Darshan Shankar is the Vice Chancellor of TDU. He was not involved in the peer review process and editorial decisions related to this paper.

Author contribution

Bhavya Vijay: Investigation, Writing-original draft preparation. Batul Diwan: Investigation, Methodology, Writing-original draft preparation. **Poornima Devkumar**: Supervision, Writing - review and editing. **Prasan Shankar**: Supervision, Writing - review and editing, conceptualization. **Chethala N Vishnuprasad**: Supervision, Writing - review and editing, Formal analysis, Conceptualization. **Gurmeet Singh**: Conceptualization, Supervision, Writing - review and editing, Formal analysis, Funding acquisition. **Deepshikha Kataria**: Investigation, Writing - review and editing. **Darshan Shankar**: Conceptualization, Supervision, Writing - review and editing.

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