

## International Research Journal of Ayurveda &amp; Yoga

Vol. 5 (12),73-81, Dec,2022

ISSN: 2581-785X; <https://irjay.com/>DOI: [10.47223/IRJAY.2022.51212](https://doi.org/10.47223/IRJAY.2022.51212)

## A comparison of Volatile Organic Compounds (VOCs) and the Concept of *Gandha* with special reference to *Balagraha*

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### Article Info

#### Article history:

Received on: 09-10-2022

Accepted on: 17-12-2022

Available online: 31-12-2022

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### ABSTRACT:

The ancient science of Ayurveda has many unique concepts regarding the creation of the living, health issues, diseases and their treatment. These are distinctive and have the scope to incorporate modern development into them. During the trying times of the recent pandemic, there has been the development of sensors for detecting VOCs (volatile organic compounds) produced by COVID-infected individuals which helped to diagnose the disease swiftly to minimize its spread. The interaction between pathogenic viruses in respiratory tract infection and the body's microenvironment produces distinctive volatile organic compounds (VOCs). VOCs are gaseous molecules released as a product of metabolic processes in the body whose composition changes directly as a result of pathologic processes, such as an infection. This concept of different body odours in physiological and pathological conditions has been mentioned in Ayurveda thoroughly, especially in the context of *Balagraha* (which can be correlated to various infectious diseases). This shows the science's proficiency to be way ahead of its time. Thus, the incorporation of such distinctive ayurvedic concepts will help in the comprehensive development of the medical sciences.

**Keywords-** Volatile organic compounds, *balagraha*, infectious diseases, *gandha*

## INTRODUCTION

Ayurveda has many remarkable concepts like *Tridosha*, *Ojus*, *Agni*, *Dhatu* etc. One of such main concepts is *Panchamahabhuta* (the five elements). The five elements include *akasha* (space), *vayu* (air), *agni* (fire), *jala* (water) and *prithvi* (earth). Ayurveda believes that everything is made of these “*Eha hi dravyam panchamahabhutatmakam*”.<sup>1</sup> There is an equilibrium which is maintained at both macrocosm and microcosm levels thus making our body a very minute image of the universe.<sup>2</sup> The various types of substances existing in the

universe are created by inter-mixing these five with each other in a special and specific manner.<sup>3</sup> The ayurvedic idea of disease and health is conceived around the *Tridosha* concept (the three body humors). These three are in turn made through a differential combination of the five elements. Health is considered as a balance of these three humors. So, any disturbance in the five elements will affect the balance of the three humors thus causing disease. Each *mahabhuta* has some special quality and one of the main senses is related to it. In this manner, the chief property of *prithvi mahabhuta* (earth element) is *kharatva* (roughness)



and *gandha* (smell) is the main sense of this *mahabhuta*.<sup>2</sup> So, the notion of smell is not alien to Ayurveda and is included as one of the basic principles of the science.

## MATERIALS AND METHODS

This article is a review of various Ayurvedic classical texts. Materials related to the concept of *gandha*, *sarira gandha* in physiological and pathological conditions, *balagrahas* and other related topics have been collected from various Ayurvedic texts. The *samhitas* used in the present study were *Charaka samhita*, *Shushruta Samhita*, *Ashtanga Sangraha* and *Astanga Hridaya* with commentaries on them. The modern medical literature on volatile organic compounds (VOCs) as well as other related information was collected from PubMed and Google Scholar databases. The references were compiled, analysed and discussed.

## DISCUSSION

### The Concept Of *Gandha*

According to Ayurveda, *indriyas* (sense organs) are the apparatus to attain knowledge for *Atma* (soul). These are eleven in number which includes 5 *gyanendriya* (sense faculties)- *chakshu* (visual apparatus), *srotra* (auditory apparatus), *rasana* (gustatory apparatus), *sparshana* (tactile apparatus), *ghrana* (olfactory apparatus); 5 *karmendriya* (motor organs)- *vaak* (organ for speech), *upastha* (reproductive part), *pani* (hands), *pada* (legs), *payu* (excretory organs); and 1 *ubhayendriya*- *mana* (mind). These *indriyas* are also made of the five elements. Each sense faculty has the dominance of one element and a particular sense organ receives only *guna* (specific attribute) of that element in the form of stimulus. For e.g. *ghranendriya* (olfactory apparatus) is dominated by *prithvi mahabhuta* (earth element) and receives knowledge of *gandha* (smell).<sup>4</sup> Acharya Charaka has further mentioned the intellectual aspect of the five *gyanendriya*. This is termed *Indriya Panchapanchaka*. It includes *indriya* (sense faculties), *indriya dravya* (material constituents corresponding to the sense faculties), *indriya adhisthana* (sense organ), *indriya artha* (objects) and *indriya buddhi* (perception). For *ghranendriya*, *bhu* (earth) is *dravya*, *nasika* (nose) is *adhisthana*, *gandha* (smell) is *artha* and *gandha buddhi* (olfactory centre in the brain) is *indriya buddhi*.<sup>4</sup> The *ghranendriya* is responsible to complete its respective work viz. transmission and interpretation of sense of smell. Further, the learning process carries on where the *ghranendriya* connects *mana* (mind) which is synchronous with *Atma* (soul) and thereafter knowledge is

perceived. This is necessary for a normal sense of smell.<sup>5</sup> Acharya Charaka, in *Indriyanikam indriya* opines that if a person fails to recognize the smell of different objects, whether good or bad or not responsive to any smell at all, it is suggestive that the person is having fatal signs related to olfactory sensation.<sup>6</sup> This shows the importance of smell as a sense in Ayurveda science.

### The Concept Of *Balagraha*

Ayurveda among its eight branches, explains a branch by the name *Graha Chikitsa*.<sup>6</sup> This *graha* includes conditions of behavioural abnormalities mainly. The concept of *balagraha* is different from it and forms a major portion of *Kaumarbhritya* (paediatrics). *Balagrahas* are mainly infectious diseases occurring in children. One of the main causes mentioned for *balagraha* invasion in a child is lack of cleanliness. This can be correlated with various infectious diseases caused because of unhygienic practices. According to mythology, *balagrahas* were created by Shiva and Parvati to protect their son.<sup>8</sup> So according to Ayurveda these *grahas* have a protective function which can be compared to lifelong immunity acquired after infection with some microorganisms. These *graha* are *agantuja* (external factors) in nature and do not cause vitiation in bodily activities initially.

### Clinical Features Of *Balagraha*

The prodromal features include continuous crying and fever.<sup>9</sup> General signs and symptoms are- fear, too much yawning, movement of eyebrows, timidity, discharge of froth from the mouth, upward gaze, biting the lips, grinding teeth (bruxism), absence of sleep, crying, moaning, aversion to breast, change of voice, scratching their own body or of mothers without any reason (irritability).<sup>10,11</sup>

### Classification Of *Balagraha*

According to different Ayurveda treatise number of *balagrahas* are as mentioned in Table 1. Other Ayurveda textbooks like *Kasyapa Samhita*<sup>14</sup> and *Harita Samhita* have also mentioned the concept of *graha*.

### Symptoms Of Specific *Balagraha*

Some of the *balagrahas* with probable infectious modern correlations and with clinical features are mentioned in Table 2. Also, the specific body odours associated with these *balagrahas* are mentioned in Table 3.

### Other Contexts Where Body Odour Is Mentioned In Ayurveda

Body odour is mentioned under various physiological and pathological conditions in Ayurveda. Some of the examples are enlisted in Table 4.

### The Concept Of Volatile Organic Compounds (Vocs)

Odours emitted from a body function as an indicator of the metabolic or psychological status of an individual. The human body emits a good array of volatile organic compounds (VOCs), both odorous and non-odorous. The VOCs emitted from different areas of the physical body vary with age, diet, sex, physiological status and possibly genetic background. Due to this, each individual has specific body odours and these can be considered 'odour-fingerprints'. Pathological processes, like infection and endogenous metabolic disorders, influence our daily odour fingerprints by producing new VOCs or by changing the ratio of VOCs that are produced normally.<sup>37</sup>The main analytical equipment for these VOCs is gas chromatography and mass spectrometers.<sup>38</sup> This was first recognised by Hippocrates around 400 BD, and he reported several disease-specific odours from urine or sputum. The major sources of VOCs include breath, sweat, skin, urine, faeces and vaginal secretions. Blood is also an important source of body odours because some metabolically produced VOCs are secreted into the blood and with time emitted out via breath and/or sweat. Some examples of such VOCs are mentioned in Table 5.

Even though covid 19 showed a low fatality rate, it was highly infectious with raw reproduction number (RO) ranging from 1.4 to 6.47. Owing to this transmissibility of the Covid infection as a pandemic, the need of the hour was to develop highly sensitive, precise, distinctive, and specific biosensor platforms. Also, the present method of analysis using RT-PCR even though is accurate but takes time to generate results and is also unpleasant on part of the patient. This led to the creation of multiplex sensors which were designed based on nanomaterials linked with organic ligands, which created a versatile sensor layer that could change its structural properties when exposed to VOCs and cause electrical resistance changes.<sup>39</sup> Since COVID-19 affects mainly the lungs, breath has been considered the most straightforward sample to analyse. The complex biochemistry processes of COVID-19 such as SARS-CoV-2 entry and replication, humoral and cellular immunity, and cytokine storm, could induce the formation of VOCs or alter the normal VOCs profiles.<sup>38</sup> Also, the infection leads to a variation of the microbial flora in the lungs and, as a consequence, to a variation of exhaled metabolites. These VOCs are the targets of breath diagnostics and are used to assess health status without being invasive for patients. The four most prominent VOCs in COVID-19 are methylpent-

2-enal, 2,4-octadiene 1-chloroheptane, and nonanal, with typical concentrations of 10 to 250 ppb.<sup>40</sup> According to a study by Shan *et al.*, the feasibility of the sensors approach was investigated with an array of nanostructured sensors that were used to analyze the breath of subjects in two Chinese hospitals. The results of this study show that sensors can discriminate against COVID-19 with respect to healthy subjects and subjects affected by other lung pathologies.<sup>41</sup> Also, scientists from the Biotech firm RoboScientific, a start-up in Cambridgeshire developed a 12-sensor device that detects the coronavirus' unique odour primarily ketone and aldehyde compounds. The device was put to test by a team from the London School of Hygiene & Tropical Medicine (LSHTM) and Durham University in the UK by using body odour samples from socks worn and donated to by 54 individuals of which 27 COVID-19 positive individuals (asymptomatic or had mild symptoms) and 27 uninfected individuals. The scientists found that the device could correctly detect the virus from the samples with an accuracy rate of between 98 and 100 per cent. Recently, ARDS among COVID-19 patients and non- COVID-19 patients were also successfully differentiated by breath VOCs profiles. Also, in a study by Steppert *et al.*, it was shown that VOC biomarkers can be successfully used to discriminate between COVID-19 and influenza-A.<sup>[42]</sup> Thus, these sensors could help in early, affordable, and accurate diagnosis, thereby easing the early intervention efforts and slowing down the pandemic's transmission. According to Sushruta, there are 6 ways to examine a disease which include examination through 5 sense organs and the sixth one is *prashna* (questioning). This shows that in Ayurveda, *gandha* along with objects of other sense organs were always considered an integral part of the diagnosis. So, the concept of *gandha* (smell) is well explained in Ayurveda. As in modern science, the concept of smell is not only related to a sense organ but is considered a type of *budhi* (intelligence) which has deep roots in understanding various aspects of the human body and so is of utmost importance in treatment also.

### CONCLUSION

The use of animals to detect body odours or the development of sophisticated sensors to identify these have been recent developments but the use of body odours to identify a disease has been carried out since time immemorable. Ayurveda being the science of life has not only explained this concept in detail but also includes it in one of the basic principles of the science. Also, this concept

was specifically highlighted while mentioning *balagraha* (infectious disease in children). Today we realise that it is due to the VOCs produced by a diseased body. This shows the in-depth knowledge embedded in the ancient science. So, acknowledging and implementing the concepts of Ayurveda will not only help mankind to live a better life but will also help the present as well as future scientists and medical fraternity to deal with catastrophes like COVID-19. Further high-end researches in the basic principles of Ayurveda will help to develop newer techniques in diagnosis and management of existing and emerging diseases.

### Acknowledgments- Nil

### Conflicts Of Interest- Nil

### Source of finance & support – Nil

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**How to cite this article:** A comparison of Volatile Organic Compounds (VOCs) and the Concept of *Gandha* with special reference to *Balagraha*”  
IRJAY.[online]2022;5(12); 73-81.  
Available from: <https://irjay.com>  
DOI link- <https://doi.org/10.47223/IRJAY.2022.51212>

**Table 1- Classification of *Balagrahas***

Susruta Samhita <sup>12</sup> Madhava Nidana Bhavaprakash Yogaratnakara <sup>13</sup> All these mention 9 <i>grahas</i>	1. <i>Skandha</i> 2. <i>Skandhapasmara</i> 3. <i>Shakuni</i> 4. <i>Putana</i> 5. <i>Andhaputana</i> 6. <i>Sheetaputana</i> 7. <i>Mukhamandika</i> 8. <i>Naigamesha</i> 9. <i>Revati</i>
Vagbhata- Mentions 12 <i>grahas</i> (Above 9+ 3)	10. <i>Swagraha</i> 11. <i>Pitrugraha</i> 12. <i>Shuskarevati</i>

**Table 2- Clinical features and probable modern correlations of *Balagrahas***

NAME OF <i>GRAHA</i>	CLINICAL FEATURES	PROBABLE CORRELATIONS
<i>SKHANDA</i> <sup>15,16</sup>	<ul style="list-style-type: none"> <li>• Unilateral lacrimation</li> <li>• Involuntary movement of the head</li> <li>• Hemiplegia</li> <li>• Hypertonicity of muscles</li> <li>• Excessive sweating</li> <li>• Drooping of head</li> <li>• Grinding of teeth/ Bruxism</li> <li>• Aversion to breast milk</li> <li>• Frightened look</li> <li>• Excessive cry with altered voice</li> <li>• Facial palsy</li> <li>• Excessive drooling of saliva</li> <li>• Rolling up of the eyeball</li> <li>• Clenching of palm</li> <li>• Constipation</li> <li>• Involuntary movement of an eye, cheek, eyebrow</li> <li>• Reddishness of bilateral eyes</li> <li>• Finally causes handicap or death</li> </ul>	Acute bacterial meningitis <sup>15</sup>
<i>NAIGAMESHA</i> <sup>17,18</sup>	<ul style="list-style-type: none"> <li>• Abdominal distension</li> <li>• Involuntary movement of limb and hand</li> <li>• Vomiting froth</li> <li>• Excessive thirst</li> <li>• Clenching of hands</li> <li>• Diarrhoea</li> <li>• Feeble sound</li> </ul>	Acute gastroenteritis <sup>17</sup> Infectious condition <sup>18</sup>

	<ul style="list-style-type: none"> <li>• Discolouration of body</li> <li>• Excessive crying/ howling</li> <li>• Vomiting breastmilk</li> <li>• Cough</li> <li>• Hiccups</li> <li>• Sleeplessness</li> <li>• Biting of lips</li> <li>• Stiffness</li> <li>• Hypertonicity of muscles</li> <li>• Rolling up of eyes</li> <li>• Smiling-like facial expression</li> <li>• Opisthotonos</li> <li>• Fever</li> <li>• Loss of sensorium</li> <li>• Monocular oedema</li> </ul>	
<i>SWAGRAHAM</i> <sup>19,20</sup>	<ul style="list-style-type: none"> <li>• Shivering</li> <li>• Horripilation</li> <li>• Excessive sweating</li> <li>• Drooping of eyelid</li> <li>• Opisthotonos</li> <li>• Biting of tongue</li> <li>• Hoarseness of voice and laryngeal spasm</li> <li>• Hyperactivity/ running around</li> <li>• Barking voice</li> </ul>	Encephalopathy <sup>19</sup> Rabies <sup>20</sup>
<i>PITRUGRAHAM</i> <sup>21,22</sup>	<ul style="list-style-type: none"> <li>• Horripilation</li> <li>• Tics</li> <li>• Frequent crying</li> <li>• Fever</li> <li>• Cough</li> <li>• Diarrhea</li> <li>• Vomiting</li> <li>• Frequent yawning</li> <li>• Thirst</li> <li>• Convulsions</li> <li>• Emaciation</li> <li>• Spasticity of muscles</li> <li>• Cyanosis/ pallor (discolouration of the skin)</li> <li>• Fist formation by the child</li> <li>• Watering eyes</li> </ul>	Acute gastroenteritis with respiratory tract infection <sup>21</sup>
<i>SAKUNIGRAHAM</i> <sup>23,24</sup>	<ul style="list-style-type: none"> <li>• Flaccidity of extremities</li> <li>• Diarrhoea</li> <li>• Ulcer on tongue, palate and throat</li> <li>• Papules/ Pustules on joints</li> </ul>	<ul style="list-style-type: none"> <li>• Yercinia colitis <sup>23</sup></li> <li>• Impetigo</li> <li>• Molluscum contagiosum <sup>24</sup></li> </ul>

	<ul style="list-style-type: none"> <li>• Arthritis</li> <li>• Excoriation on anal region and buccal cavity</li> <li>• Frightened look</li> <li>• Fever</li> <li>• Smell of birds</li> </ul>	
<i>REVATHI</i> <sup>25,26</sup>	<ul style="list-style-type: none"> <li>• Cyanosis</li> <li>• Rubbing of eyes, ears and nose</li> <li>• Cough</li> <li>• Hiccups</li> <li>• Blinking of eyes</li> <li>• Deviation of mouth to one side</li> <li>• Redness of oral cavity</li> <li>• Fever</li> <li>• Emaciation</li> <li>• Stool of greenish colour and loose consistency</li> </ul>	Intra-uterine infections like TORCH <sup>26</sup>

**Table 3- Specific Body Odour Associated with Each *Balagraha***

NAME OF GRAHA	SMELL	
	SUSHRUTA	ASHTANGA HRIDAYA
<i>SKHANDA</i> <sup>15,16</sup>	<i>Kshata</i> (Smell of blood)	<i>Vasa asra</i> (Muscle fat and blood)
<i>NAIGAMESHA</i> <sup>17,18</sup>	<i>Vasa</i> (Smell of muscle fat)	<i>Bastha</i> (Smell of goat)
<i>SWAGRAHAM</i> <sup>19,20</sup>	-	<i>Vit</i> (Smell of faeces)
<i>PITRUGRAHAM</i> <sup>21,22</sup>	-	<i>Shava</i> (Smell of Cadaver)
<i>SAKUNIGRAHAM</i> <sup>23,24</sup>	<i>Vihaga</i> (Smell of bird)	<i>Shakuni</i> (Smell of bird)
<i>REVATHI</i> <sup>25,26</sup>	-	<i>Bastha</i> (Smell of goat)



**Table 4- Body odours mentioned in different contexts in various Ayurvedic treatises**

Chapter	Context	Smell	Modern Correlation	Reference
<i>Prameha</i>	<i>Kshara prameha</i>	<i>Gandha like kshara</i>	Smell like alkaline	(27)
<i>Rogabhishakjitiya</i>	<i>Pitta prakriti</i>	<i>Visra prabhut pootika</i>	Foul putrified smell	(28)
<i>Jwara</i>	<i>Mamsastha</i>	<i>Dourgandha</i>	Foul smell	(29)
<i>Kushta</i>	<i>Paitika kushta</i>	<i>Visra gandha</i>	Foul smell	(30)
<i>Unmada</i>	<i>Asadhya</i>	<i>Pootigandha</i>	Putrified smell	(31)
<i>Arsa</i>	<i>Pitta arsa</i>	<i>Visragandhi raktasravi</i>	Foul smell blood discharge	(32)
<i>Raktapitta</i>	<i>Poorvarupa</i>	<i>Loha lohitya matsya aama gandha aasyata</i>	The oral cavity smells of metallic, blood, fishy, undigested	(33)
<i>Mootraghata</i>	<i>Poorvarupa</i>	<i>Basthagandha mootra</i>	Urine smells like goat	(34)
<i>Mootraghata</i>	<i>Vitvighata</i>	<i>Vit tulya gandha mootra</i>	Urine has the smell of faeces	(35)
<i>Pandu</i>	<i>Pitta pandu</i>	<i>Dourgandhya</i>	Foul smell	(36)

**Table 5- Volatile Organic Compounds (VOCs) associated with various disease conditions**

Disease	Source	Odour	Volatile compound
Cholera	Faeces	Sweetish	Dimethyl disulphide, p-menth-1-en-8-ol
Advanced breast cancer	Affected area	Rotting	Dimethyl trisulphide, fatty acids
Advanced head-and-neck cancer	Affected area	Rotting	Dimethyl trisulphide, fatty acids
Gynaecological tumours	Tumour	Rotting	Volatile fatty acids
Phenylketonuria Isovaleric	Sweat, urine, infant skin	Musty, sweaty locker room towels	Phenylacetic acid
Methionine malabsorption syndrome Hypermethioninemia	Skin, urine	Malt, hop	a-Hydroxybutyric acid Dimethyl
Diabetes/diabetic ketoacidosis	Breath	Rotten apple, acetone-like	Acetone, other ketones
Liver disease	Breath	Malodour	C2-C5 Aliphatic acids, methylmercaptan
Hepatic encephalopathy	Blood	Amine	3-Methylbutanol