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Philosophy of Complimentary Healing of COVID-19 Remedies Practiced in Varied Communities of Manipur State, Northeastern India: A Review

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Abstract

In the study of complimentary healing of COVID-19 remedies, 41 traditional disease complexes were treated by 10 different routes of administration using 19 mono-ingredient and 7 multi-ingredient compositions. Preparation methods included boiling in water (28%), burning the materials (48%), crushing the materials to release the aroma (21%) and slight heating of the materials (3%). Some of the mono-ingredient recipes reported in the study were observed to have similar uses in other parts of the world, whereas poly-herbal remedies were found to be unique without any similar report. Scientific characterization of the herbal remedies can contribute to the endorsement of traditional vapour-based therapies in the modern health care systems. Findings from these "new usage" reports of plants and unique combinations of poly-herbal compositions indicate the importance of such documentation efforts.

Keywords: COVID-19; Complimentary Healing; Mono-Ingredient and Multi-Ingredient; Herbal Remedies

1. Introduction

Currently, the search to identify treatments and vaccines for novel coronavirus disease (COVID-19) are ongoing. Desperation within the community, especially among the middle-and low-income groups acutely affected by the economic impact of forced lock-downs, has driven increased interest in exploring alternative choices of medicinal plant-based therapeutics. This is evident with the rise in unsubstantiated efficacy claims of these interventions circulating on social media. Based on inquiries received, our team of researchers was given the chance to produce evidence summaries evaluating the potential of complementary interventions in COVID-19 management. Here, we present and discuss the findings of four selected medicinal plants (*Nigella sativa*, *Vernonia amygdalina*, *Azadirachta indica*, *Eurycoma longifolia*), with reported antiviral, anti-inflammatory, and immune-modulatory effects that might be interesting for further investigation. Our findings showed that only *A. indica* reported positive antiviral evidence specific to the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) based on preliminary *in silico* data while all four medicinal plants demonstrated differential anti-inflammatory or immune-modulatory effects. The definitive roles of these medicinal plants in cytokines storms and post-infection complications remains to be further investigated. Quality control and standardization of medicinal plant-based products also need to be emphasized. However, given the unprecedented challenges faced, ethno-pharmacological research should be given a fair amount of consideration for contribution in this pandemic.

The emergence of a new corona virus, known as the SARS-CoV-2 has initiated a pandemic of COVID-19 [1,2]. More than 31 million infections with at least 960,000 COVID-19 associated deaths were reported by September 23, 2020 [3]. Since its first reported case in Wuhan, China in December 2019 [3] (WHO, 2020c), new discovered evidence by both clinicians and researchers globally have helped shed some light on the disease pathogenesis and the nature of the virus itself.

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2. Literature Review

The availability of new information subsequently fed policy changes on transmission prevention strategies as well as development of preventative vaccines and therapeutic drug candidates. Enforced physical distancing, hand hygiene, and arguably proper usage of personal protective equipment including wearing a surgical mask remains the most effective way of controlling the spread of the disease, with most countries which adopted such measures reporting some success in curbing the disease spread [4, 5]. However, several challenges remain in maintaining these drastic measures of enforced physical distancing for long periods of times. Resurgences of infection waves were reported in few countries after the relaxation of rules. In addition, the economic impact of prolonged lock down on social issues such as loss of income and increased poverty, especially for the low and middle-income countries, is evident [6,7].

As the world looks towards science in search of an effective drug or vaccine, a few countries, such as China and India, with long histories of traditional medicine use [8, 9] have also started exploring the role of traditional and complementary, alongside conventional treatment. The Malaysian community, coming from a tropical multi-racial country rich in flora and fauna, also appears to be interested in venturing towards the use of herbal and complementary medicine, some of which are based on local traditional knowledge. During the Movement Control Order implemented by the Malaysian Government in March 2020 in attempts to curb the disease spread, the herbal medicine research arm of biomedical research institute in Malaysia has received numerous queries on the potential use of complementary remedies including single medicinal plants, traditional remedies, finished herbal products, supplements, food products, and medical devices against COVID-19. These queries were mainly submitted directly by the public and persons with readily available herbal products or identified through highly circulated messages on several social media platforms.

3. Methods

To survey and document the plant species associated with vapour therapy in Manipur, Northeast India, and to evaluate these traditional practices. Semi-structured questionnaires were used to collect information from the *Meitei* community in the Imphal valley and the Jiribam area in Manipur. Traditional disease concepts were studied along with their corresponding medical terminologies. Plant samples collected from fields; healers' private collections and home gardens were identified. Evaluation of the ethnobotanical data was performed with a modified fidelity level index.

Communities of Manipur: When Manipur State became a part of Indian sub-continent in 1949, 29 communities were recognised as Scheduled Tribes (ST) under the Indian Constitution. They are Aimol, Anal, Angami, Chiru, Chothe, Gangte, Hmar, Kabui, Kacha Naga, Koirao, Koireng, Kom, Lamkang, Mao, Maram, Maring, Mizo, Monsang, Moyon, Paite, Purul, Ralte, Sema, Simte, Shalte, Tangkhul, Thadou, Vaiphei and Zou. In 2003, four more communities viz., Kharam, Paomai, Songthu, and other Kuki Tribes were added to the ST list increasing the number up to 33.

From March to September 2020, 22 interventions of interest were reviewed through searches conducted on electronic databases such as Pub-med, Web of Science, Google Scholar; as well as hand searching of grey literature, including books on herbal and traditional medicine available in institutional library resources. The predetermined search terms used are 'COVID-19', 'antiviral', 'anti-inflammatory', 'immune system', 'immune modulatory', 'safety', 'toxicity', in combination with the name of the main intervention of interest or its synonyms. From these evidence summaries, five were single medicinal plants including *Azadirachta indica* A.Juss, *Eurycoma longifolia* Jack, *Nigella sativa* L., *Gymnanthemum amygdalinum* (Delil) Sch. Bip. (or *Vernonia amygdalina* Delile), and *Mitragyna speciosa* (Korth.).

Four medicinal plants (*A. indica*, *E. longifolia*, *N. sativa*, and *V. amygdalina*) discussed here collectively exhibited pleiotropic effects which can potentially provide a multi-modal approach via antiviral, anti-inflammatory, and immune modulatory effects in COVID-19 management. At present, it is evidently challenging to pool data from published studies due to variation in extracts selection and a lack of well-reported standardization data of the investigated formulations. Still, it is quite clear that there is insufficient evidence of direct antiviral effects specific to the SARS-CoV-2. Further investigations on differential anti-inflammatory and immune modulatory effects as well as quality and safety of herbal medicines are required to ascertain their role in COVID-19 management.

In Global context, before the investigation of medicine in the form of tablets, ointments, syrup, vaccine, injections, etc. human beings at the very outset, use the easiest method of medicine in the form of traditional medicine (TM) which are prepared in liquid, solid, semi-solid or gas states. The use TM in the form of powders, vapours, smokes or volatile oils for treatment of many types of ailments has made administration of gaseous medicine a popular therapy in TM.

Vapour-based therapies have been reported in many cultures and form an integral part of health care systems all over the world [10, 11]. With respect to plant derived medicinal smoke alone, there are more than 1000 use reports from over 737 plants throughout the world [11]. Application of vapour-based medicine as part of traditional medicine has been reported in Africa [10, 12], Australia [13], America [14, 15], Europe [16] and Asia [17, 18]. The anti-inflammatory activity of cannabinoids may compromise host inflammatory responses to acute viral infections [19]. However, it may be beneficial in persistent infections and the effect of cannabinoids and their antagonists in viral infections.

On the 18th of December 2002 the Parliament of India passed a bill under the title "The Scheduled Castes and Scheduled Tribes order (Amendment) Act 2002" The bill received the assent of the President of India on 7th January 2003. Again, on 29th October 2009, the Union Cabinet approved the inclusion of the following tribes of Manipur in the ST list viz., Inpui, Liangmei, Rongmei, Thangal, Zeme, and Mate. Apart from the 39 recognized tribes, there are other communities that are trying to be recognized as ST. Meanwhile, these communities are grouped with the community that has the closest linguistic and cultural affinity. Some small communities are already losing their uniqueness as they are being merged with bigger groups.

4. Vapour Therapy

- Plant material simply boils, and vapor is inhaled or make body massage.
- Dried plant parts simply burnt, and the smock inhaled or made fresh the air

Decoction and fresh extraction are the commonly used preparation of medicine of both Mono-herbal and Poly-herbal application of plants for COVID-19 medicine.

Vapour therapy (VT):

- VT-I: Preparation methods included boiling in water,
- VT-II: burning the materials,
- VT-III: crushing the materials to release the aroma
- VT-IV: slight heating of the materials and
- VT-V: mixed with other oil forms

Some of the mono-herbal (mono-ingredient recipes) reported in the study were observed to have similar uses in other parts of the world. Whereas polyherbal (poly-ingredient recipes) were found to be unique without any similar report.

5. Results and Discussion

In the study, 41 traditional disease complexes (Table 1) were treated by 10 different routes of administration under categories of disease complexes treated by vapour-based medicines (Fig. 1) using 19 mono-ingredient (Table 3) and 7 multi-ingredient compositions (Table 2). Preparation methods included boiling in water (28%), burning the materials (48%), crushing the materials to release the aroma (21%) and slight heating of the materials (3%) (Figure 3). Some of the mono-ingredient recipes reported in the study were observed to have similar uses in other parts of the world, whereas polyherbal remedies were found to be unique without any similar report. Various types of therapeutic applications to the patients were performed (Figure 2). They are presented in 13 applications: Steam sauna (9%), Aroma inhalation (22%), Steam inhalation (9%), Smoke inhalation (29%), Steam fomentation (1%), Steam directed at the anal region (8%), Smoke directed at whole body (1%), Steam directed at the urinogenital region (1%), Smoke directed at the mouth (2%), Smoke directed at the anal region (11%), Smoke blown into the nose (1%), Smoke blown into the ear (1%) and Ambient smoke (3%), etc.(Figure 2).

For polyherbal remedies seven plant parts were mixed up and the decoction is applied to the patient three-times daily by the *Kabui* Tribe of Manipur (Table 1). It is the first of its kind got information from the *Kabui* Tribe of Manipur.

Table 1 Traditional disease concepts with matching modern medicine terminologies**.**

SL No	Traditional disease or symptom complex	Equivalent modern medicine concept
1.	Amangba yeikhatpa	Constipation
2.	Arum laihou	Malaria
3.	Asinba kaba	Acidity
4.	Bhukuti (Khulai laihou)	Pneumonia

5.	Dhatu nai taba	Gonorrhea
6.	Ee nungsit na chikpa	Dysmenorrhea
7.	Ee-nungsit	Irregular mensuration
8.	Hara thungba	Asthma
9.	Khoirai	Migraine
10.	Khou naba	Tonsilitis
11.	Khouri naba	Pharyngitis
12.	Kok chikpa	Headache
13.	Kokta e nungsit haigatpa	Menstrual migraine
14.	Lai thokpa	Smallpox
15.	Lok kangkhu	Cough (Dry)
16.	Lok khuba	Cough
17.	Lok khulai	Influenza
18.	Lok na nakong yeisinba	Eustachian tube dysfunction by Cold
19.	Lok thungba	Common cold
20.	Meining kumbaa	Protective application in postpartum stage
21.	Nahi taba	Nosebleed
22.	Nakong laikhul	Otorrhea
23.	Nap taba	Rhinorrhoea
24.	Naton da til leiba	Nasal myiasis
25.	Naton makhun gi laina	Sinusitis
26.	Natonchabi	Relapsing polychondritis
27.	Natun phunba	Nasal catarrh
28.	Nungsang	Haemorrhoids
29.	Nungsang pere khaotaba	Internal haemorrhoids with rectal prolapse
30.	Nungsang pere nai chaba	Internal haemorrhoids with suppuration
31.	Patpa	Ulcerous lesion
32	Phugri	Pustules
33.	Salmit	Nasal schistosomiasis (in Cow)
34.	Sarei houba	Epilepsy
35.	Souja da mareng mareng chatpa	Pruritus ani
36.	Taaki	Syphilis
37.	Thabak phunba kheba	Wheezing
38.	Thabak ta lok leiba	Bronchitis
39.	Thagokpa	Hiccough
40.	Unsagi laina	Skin disease
41.	Ya til chaba	Dental caries

SOURCE: Ningthoujam, S.S., Talukdar, A.D., Singh, P.K. and Choudhury, M.D. (2013). Traditional use of herbal vapour therapy in Mnaipur, Northeast India: An ethnobotanical survey. Journal of Ethnopharmacology, 147: 136- 147.

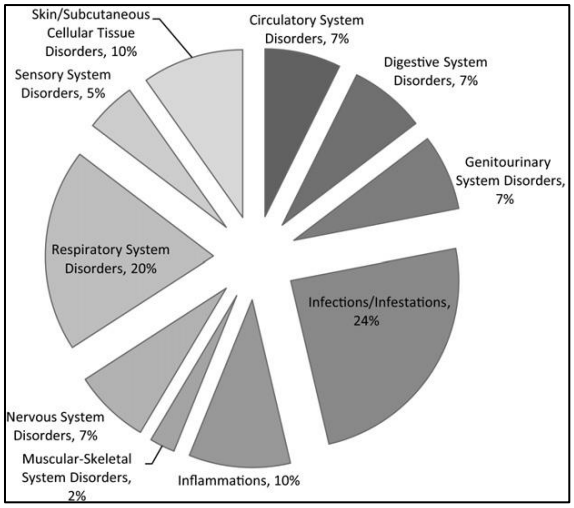

Figure 1 Categories of disease complexes treated by vapour-based medicines.

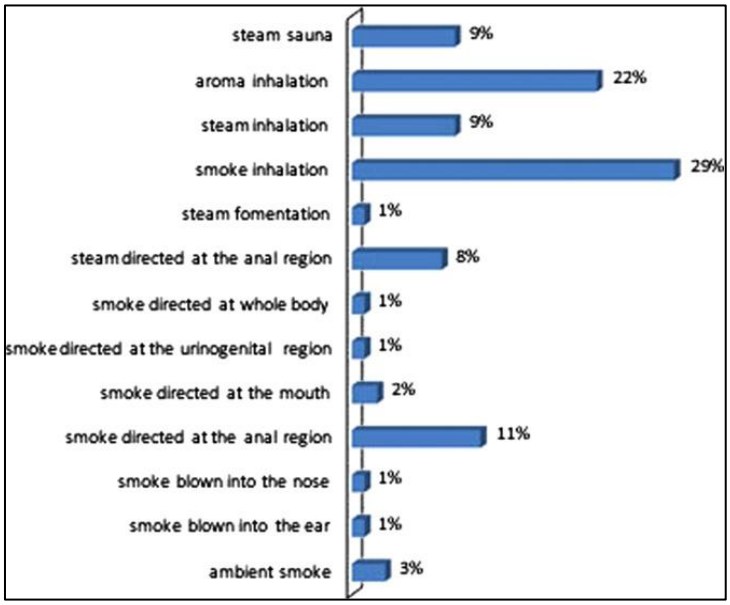

Figure 2 Various types of therapeutic applications to the patients.

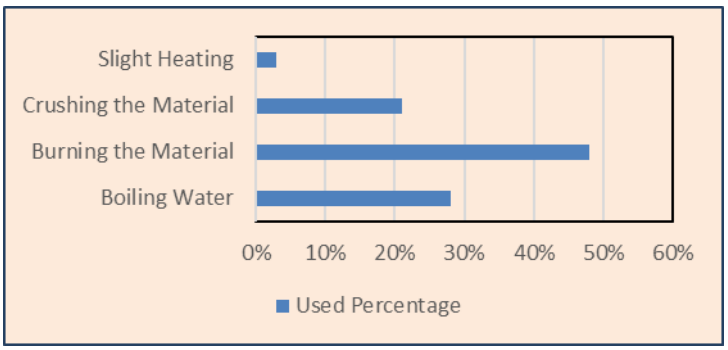

Figure 3 Preparation methods indicating the used percentage.

Table 2 Plants used selectively as multi-herbal/poly-herbal for the preventive measures of COVID-19 by *Kabui* Tribe of Manipur

Sl No	Plant name	Family	Local name	Part used
1.	*Eleusine indica* (L.) Gaertn.	Poaceae	Manipuri : *Pungphai ;* Hindi : *Makra ;* Kabui : *Gak-Cup*	Decoction of leaves, young twigs including inflorescence
2.	*Eupatorium cannabinum* L.	Compositae	Common Name: *Hemp Agrimony* Assamese; *Tongol-lati*; Manipuri: *Langthrei-Khongnembi;* Kabui: *Lengleiton*	Decoction of leaves, young twigs
3.	*Isodon ternifolius* (D.Don) Kudô;	Lamiaceae	Manipuri: *Khoiju;* Kabui: *Khamneo;* Kabui: Chothe: *Khoichu*	Decoction of leaf and inflorescence
4.	*Mellotus philippensis* (Lam,) Mull. Arg.	Euphorbiaceae	Common Name: *Monkey Face Tree, Kamala tree, Red Berry*; Manipuri & Kabui: *Ureirom Laba,* Thadou: *Hummahsan;* Paite: *Hummuhsan.*	Decoction of Leaf
5.	*Pinus kesiya* Royale ex Gordon	Pinaceae	Common Name: *Khasi Pine, Banquet Pine*; Manipuri & Kabui: *Uchan*; Tangkhul: *Mafra, Matangthing*; Thadou: *Taksing*; Paite: *Taksing*; Liangmei: *Kalu Sing*; Rongmei: *Lai Baang*; MIzo: *Far*	Wood boil water
6.	*Schefflera arboricola* (Hayata) Merr.	Araliaceae	Common Name: *Dwarf Umbrella Tree*; Manipuri: *Laikhut* ; Kabui: *Tarang*	Decoction of Leaf
7.	*Schoenoplectus lacustris* (L.) Palla	Cyperaceae	Common Name: *Great Bulrush*; Manipuri: *Kouna;* Kabui: *Dam*	Decoction of the aerial portion of the plant

Table 3 Plants used selectively as mono-herbal for the preventive measures of COVID-19 *Manipuri* Community of Manipur

Sl No	Plant name	Family	Local name	Part used
1.	*Alangium chinense* (Lour.) Harms	Alangiaceae	Common Name: *Chinese Alangium;* Assamese & Bengali:*Marli, Bhelu; Manipuri*: *Kokal;*	Decoction of the leaves
2.	*Premna mollissima* Roth	Lamiaceae	Common Name: *Dusky Fire Brand Teak, Broad Leaf Premna;* Manipuri: *Upongtha, Linbui;* Anal: *Linsui,* Hindi: *Baker,* Bangali: *Gohara,* Assamese: *Gonderi*	Leaf and root decoction
3.	*Terminalia arjuna* (Roxb. ex DC.) Wight & Arn.	Combretaceae	Common Name: *White Murdoh, Arjun Tree;* Manipuri: *Mayokpha;* Paite: *Vandotsing*	Decoction of Leaf and Wood Bark
4.	*Acorus calamus* L.	Acoraceae	Common Name: *Sweet Flag;* Manipuri: *Okhidak*; Thadou: *Vohluthao;* Mizo: *Hnim-Rimtui;* Mao: *Donia;* Paomei: *Vassiipro; Seihraipeu:*Chothe: *Anoi Bu;* Maram: *Abakha*	Decoction of Leaves with Rhizome

5.	*Allium ascalonicum* L.	Amarillidaceae	*M. Meitei Tilhou*	Leaves and bulbs
6.	*Allium cepa* L.	Amarillidaceae	*C. Onion, M. Tilhou, H. Piyaz, B. Pyanj*	Leaves and bulbs
7.	*Allium sativum* L.	Amarillidaceae	*M. Chanam, C. Garlic, H. Lasan,B. Lasun*	Leaves and bulbs
8.	*Canabis sativa* L.	Cannabinaceae	Manipuri: *Nongpok-lei; Ganja;* Common Name: *True Hemp, Marijuan;*, Hindi & Bengali: *Bhang, Ganja*	Leaves and mature twig
9.	*Cinnamomum tamala* Nees	Lauraceae	Manipuri: *Tejpat*	Leaves
10.	*Curcuma longa* L.	Zingiberaceae	*M. Yaingang*	Rhizome fresh or boiled
11.	*Houttuynia cordata* Thunb.	Saururaceae	*M. Tokningkok*	Leaves and roots
12.	*Melia azedarach* L.	Meliaceae	*C. Pride of India, China tree, Baksin tree Persian liliac, M. Seijrak, H.Drek,A.Thamaga,B.Mahanim*	Leaves
13.	*Ocimum tenuiflorum* L.	Lamiaceae	Common Name: *Sacred basil,* Manipuri: *Tulsi*	Leaves and tender shoot with inflorescence
14.	*Phlogacanthus thyrsiflorus* (Roxb.) Nees	Acanthaceae	Manipuri: *Nongmangkha*	Leaves and inflorescence
15.	*Rhus chinensis* Mills.	Anacardiaceae	*M. Heimang, H. Tari, A. Naga-tenga*	Tender leaves and fruits
16.	*Zingiber officinale* Rosc.	Zingibeaeceae	Common Name: Ginger; Manipuri: *Shing*	Rhizome
17.	*Pinus kesiya* Royale ex Gordon	Pinaceae	Common Name: *Khasi Pine, Banquet Pine*; Manipuri & Kabui: *Uchan*; Tangkhul: *Mafra, Matangthing*; Thadou: *Taksing*; Paite: *Taksing*; Liangmei: *Kalu Sing*; Rongmei: *Lai Baang*; MIzo: *Far*	Wood boil water
18	*Polygonum posumbu* Buchanam-Hamilton ex D.Don	Polygonaceae	Manipuri: *Phakpai*	Leaves and tender twigs
19.	*Zanthoxylum acanthopodium* DC.	Rutaceae	Manipuri: *Mukthrubi,* Rongmei: *Raryum, Tangang,* Hindi: *Darmar,* Bengali *Tombul*	Leaves, inflorescence and fruits

Ethnopharmacological relevance: Vapour-based medicines are an aspect of traditional medicine in Northeast India. However, no collective studies on this therapy in the region have been attempted. With the changing perception of traditional knowledge, documenting these herbal preparations and the subsequent development of baseline data for applications in further ethnopharmacological research are needed. In the study, 41 traditional disease complexes were treated on the basis of traditional disease concepts with matching modern medicine terminologies (Table 1) by 10 different routes of administration (Figure 1) using 19 mono-ingredient (Table 3) and 7 multi-ingredient compositions (Table 2) and **v**arious types of therapeutic applications were made (Figure 2). Preparation methods included boiling in water (28%), burning the materials (48%), crushing the materials to release the aroma (21%) and slight heating of the materials (3%). Some of the mono-ingredient recipes reported in the study were observed to have similar uses in other parts of the world, whereas polyherbal remedies were found to be unique without any similar report. Scientific characterisation of the herbal remedies can contribute to the endorsement of traditional vapour-based therapies in the

modern health care systems. Findings from these ‘‘new usage’’ reports of plants and unique combinations of polyherbal compositions indicate the importance of such documentation efforts.

There is a holistic approach by Traditional and religious remedies in this modern world as a plausible options, preventive and treatment of COVID-19 especially in Africa and Asia [20]. They conducted 18 mobile telephonic interviews of women aged 27–57 years and mentioned that, how women and community members successfully dealt with to understand the suspected symptoms and treatments of COVID-19 in Mwanza, Tanzania. Women folk after interview gave their remarks on 19 medicinal plants, which were used in the preparation of remedies along with honey (*Eucalyptus globulus* Labill., *Citrus limon* L.), *Azadirachta indica* A.Juss, *Psidium guajava* L., *Cymbopogon citratus* Stapf., *Ocimum gratissimum* L., *Pennisetum purpureum* Schumach., *Tetradenia riparia* (Hochst., *Zingiber officinale* Roscoe, *Allium cepa* L. and *Allium sativum* L., and some plants were crushed or boiled and the steam for inhalation through nose or mouth.

A novel concept has formulated covering the ancient means of traditional medicines or herbal medicinal plants for the treatment of COVID-19 pandemic [21]. There is a wide scope of herbal medicines that have been used since traditional times. They have been considered as potent clinical agents against wide array of viral diseases due to their anti-viral properties. These natural products of Ayurveda are being tested for treating COVID-19. Basically, these formulations are comprised of huge number of phytochemicals such as terpenoids, alkaloids, flavonoids, phenols, tannins, polyphenols, saponins, polysaccharides, proteins, lipids and peptides that possess myriads of functions against viral invasion, penetration, replication, expression, assembly and release. Moreover, medicinal plants and their natural ingredients proved to be the most promising alternatives to prevent or cure the infection and spread of this disease since its outbreak.

Many compositions mentioned in the paper are still used by the *Meitei* community. Traditional healers follow their own criteria for selecting medicinal plants. Plants recorded in this ethno-botanical study can suggest methods for selecting and identifying potentially effective plants for future drug candidates. Scientific characterization of the herbal remedies can contribute to the endorsement of traditional vapour-based therapies in the modern health care systems. Findings from these ‘‘new usage’’ reports of plants and unique combinations of poly-herbal compositions indicate the importance of such documentation efforts.

Vapour Therapy of plants were investigated in mono-herbal and poly-herbal criteria, used by the *Meitei* community of Manipur, Northeastern India [22]. Traditional healers follow their own criteria for selecting medicinal plants. Plants recorded in this ethno-botanical study can suggest methods for selecting and identifying potentially effective plants for future drug candidates. Scientific characterization of the herbal remedies can contribute to the endorsement of traditional vapour-based therapies in the modern health care systems. Findings from these ‘‘new usage’’ reports of plants and unique combinations of poly-herbal compositions indicate the importance of such documentation efforts.

But research is in the pipeline to untangle their potential positive aspect, and we expect these studies to be conducted in a more elaborated manner in future. Yet, many scientists are still engaged in these studies to develop a suitable antidote for this virus. The future possibilities uphold the fact that by combining these studies with effective technology and testing we can demonstrate their role in blocking the life cycle of this virus, protein denaturation of receptor proteins and role of certain proteases enzymes could be studied.

Our review projected the possible role of herbal plants and their sources in the treatment of COVID-19 infections due to its bioactive ingredients acting as substantial warriors in this battle. Intriguingly, pro-active devotions in this research would enable us to develop vaccines or drugs to cure COVID-19, for which it is pre-requisite to unlock this treasure of information pertaining to traditional medicines. However, there is an urgent need to invest time on these studies for acquiring about appropriate doses and formulations for discovering drugs or vaccines from these formulations. For this purpose, scientific evidence and comprehensive pharmaco-dynamic knowledge related to medicinal plants should be made available to scientists to design clinical trials. Integration of this concept would certainly develop the drug therapy soon. All what we can do is wait for the hope of radiance at the terminating point of the tunnel, in solitude.

When a host is infected with a virus, there is a dynamic competition between the ability of the host to first marshal innate (hours to days) and then adaptive immunity (>7 days post infection) vs. the replication and spread of the virus first within the host and then to additional susceptible individuals. When a virus can out-pace the containment efforts, the host may succumb. Pathology may result from damage to tissues by viral-induced cellular apoptosis or necrosis, or alternatively, host immune responses may result in immunopathology or the perceived symptoms of the infection. If, however, innate and adaptive immunity successfully suppress viral replication, specific life-long immunity may result.

The anti-inflammatory activity of cannabinoids may compromise host inflammatory responses to acute viral infections [19]. However, it may be beneficial in persistent infections and the effect of cannabinoids and their antagonists in viral infections. Cannabinoids have been used both recreationally by groups of people who have viral infections, and experimentally by scientists investigating their impact in vitro or in animal models. Cannabinoids are profoundly anti-inflammatory and impair many Ca2+-dependent enzyme systems which are central to inflammatory and cell-autonomous antiviral responses. When viral-induced host responses lead to immunopathology, as is seen in a rodent model of multiple sclerosis, TMEV-IDD, or in a persistent infection of the central nervous system caused by a non-lytic virus, BDV, cannabinoid treatment was beneficial.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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