

## Complementary and alternative medicines use in COVID-19

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1 **[Commentary]**

2

3 **Complementary and alternative medicines use in COVID-19: a global perspective on**  
4 **practice, policy and research**

5

6 **Introduction**

7 Since the first cluster of cases identified in December 2020 in Wuhan China, COVID-19 was  
8 declared a global pandemic in March 2020. As of April 2021, the pandemic has caused over 3  
9 million deaths globally.<sup>1</sup> Currently, the approved vaccines and public health prevention measures  
10 such as social distancing, hand hygiene, contact tracing, and lockdown policies remain the  
11 mainstay of COVID-19 mitigation measures.

12

13 While the emergence of effective vaccines has offered the Governments, scientific communities,  
14 and members of the public a hope out of the pandemic, effective pharmacotherapy, including  
15 immunotherapy for COVID-19 prevention and treatment, is yet to be established. Some of the  
16 early treatments recommended for COVID-19 treatments, including hydroxychloroquine, and  
17 remdesivir have demonstrated limited effectiveness in early clinical trials.<sup>2,3</sup> Currently, steroids,  
18 including dexamethasone, remain the only treatment proven to be effective in clinical trials in  
19 terms of mortality and hospitalization outcomes.<sup>4</sup> Patients and members of public across the  
20 world are known to be relying on self-care practices including the use of Complementary and  
21 Alternative Medicines (CAM) for COVID-19 prevention and symptoms relief.

22

23 CAM refers to broad sets of practices, which are not fully integrated into the dominant healthcare  
24 system and can include herbal treatments, yoga, and relaxation techniques.<sup>5</sup> These have been  
25 used by diverse communities across the world for thousands of years for the prevention and  
26 treatment of long-term health conditions and acute illnesses such as the treatment of respiratory  
27 infections. A recent systematic review of CAM use in diabetes listed over 37 different CAM types  
28 and 223 herbs used by patients.<sup>6</sup> It is estimated that up to 70% of the low and middle-income  
29 countries (LMICs) are known to rely partly or entirely on the use of CAM to treat their health  
30 problems.<sup>7</sup> Over 50% of the 194 WHO member states are currently known to have a national  
31 policy on CAM use (WHO).<sup>8</sup>

32

33 Given the lack of adequate pharmacotherapeutic approaches to COVID-19, a surge in demand  
34 for the information and CAM products has been noted in the popular media. A recent study on  
35 the impact of the COVID-19 pandemic on clinical pharmacy practice suggested pharmacists  
36 being increasingly requested information about dietary supplementation, vitamins, and any  
37 options on the shelves that could offer symptom relief and boost immune system.<sup>9</sup> This narrative  
38 will aim to discuss global practices and policies in regards to CAM use in COVID-19. A global

39 update will enable understanding of international practices and policies, patient and consumer  
40 behaviors, identification of popular CAMs and those tipped for potential benefits, including  
41 evidence base, and thereby support counselling and communications by healthcare  
42 professionals when patients present for advice. The following section will summarize information  
43 relevant to different geographical regions with a historical, religious, and cultural association with  
44 CAM use.

45

## 46 **China**

47 Traditional Chinese Medicines (TCM) have been utilized extensively in treating COVID-19  
48 patients in China during the outbreak. Personalized treatment through syndrome differentiation,  
49 unique characteristics of TCM, is appealing to clinicians. Syndrome differentiation is a summary  
50 of the pathological signs of the body at a specific stage during disease development, based on  
51 the synthesized data collected with the four diagnostic methods: observation, listening and  
52 smelling, asking, and palpation and pulse-taking.<sup>10</sup> Thus, TCM is recommended as a COVID-19  
53 treatment option in the China National Health Commission (NHC) guidelines.<sup>11</sup>

54

55 Currently, 15 TCMs are recommended with seven oral formulations (Angong Niuhuang, Zixue,  
56 Huoxiang Zhengqi, Jinhua Qinggan, Lianhua Qingwen, Shufeng Jiedu, and Fangfeng  
57 Tongsheng), and eight injectable formulations (Xiyanping, Xuebijing, Reduning, Tanreqing,  
58 Xingnaojing, Shenfu, Shengmai, and Shenmai). The China Food and Drug Administration  
59 (CFDA) has approved Xuebijing with a treatment indication of ‘new coronavirus pneumonia with  
60 severe and critical systemic inflammatory response syndrome or/and multiple organ failure’, and  
61 Lianhua Qingwen with a new indication of ‘treating for fever, cough, and fatigue caused by the  
62 light and ordinary types of the new coronavirus pneumonia.’<sup>12</sup> Each TCM formulation contains  
63 several active ingredients with proven multi-target effects, making it challenging to develop drug  
64 resistance. Many TCM formulations also possess potent anti-inflammatory and  
65 immunomodulatory effects. TCM clinical pharmacists play an active role in reviewing TCM  
66 prescriptions, preparing TCM decoctions, therapeutic monitoring, patient education, science  
67 popularization, and clinical research.<sup>13</sup> Numerous trials are currently taking place in China  
68 assessing the effectiveness of the products in COVID-19 treatment.<sup>14</sup>

69

## 70 **South Asia**

71 The use of CAM is widespread and is culturally embedded in the countries belonging to the  
72 South Asian region, including Pakistan, India, Bangladesh, Nepal, Sri Lanka, Afghanistan,  
73 Bhutan, and Maldives.<sup>15-17</sup> A study from the COVID-19 isolation center in India suggested that  
74 over a quarter (25.8%) of patients used CAM during their treatment and afterwards.<sup>18</sup>  
75 CAM practices prevalent in the area include Ayurveda, Unani, Reiki, Homeopathy, Biochemistry,  
76 and Aromatherapy. For example, since the beginning of the Indus civilization, Pakistan has a

77 long history of using herbal medicines. Up to 80% of the population use CAM, including herbal  
78 products, in their daily practice.<sup>16</sup> Traditional medicine-based therapy, including Unani and  
79 homeopathic systems, is considered a vital source of healthcare in the region, especially in rural  
80 areas, where CAM serves as the first line of therapy.<sup>15, 16</sup>

81

82 Culture, lack of access to modern medicines, and cost considerations are essential factors of  
83 CAM use in South Asia. CAM is embedded in the policy and healthcare practices in the region.  
84 For example, in 2001, “Traditional and Complementary Medicines” was included and adopted in  
85 Pakistan’s National Health Policy.<sup>8</sup> The Indian Ministry of Health has established the Ayurveda,  
86 Yoga, Unani, Siddha, and Homeopathy, namely AYUSH (Ayurvedic, Yoga, and Naturopathy,  
87 Unani, Siddha, and Homeopathy) department that was later formed as Ministry of AYUSH in  
88 2014 which has produced specific COVID-19 prevention and treatment guidelines for CAM  
89 practitioners.<sup>19</sup> The guidelines advocate the use of yoga and herbal products such as *Embilica*  
90 *officinalis* (Indian gooseberry), *Ocimum tenuiflorum* (basil) and some branded herbal formulations  
91 as immune boosters. Other herbs of relevance in South Asia include curcumin, quinine, and  
92 echinacea for their respective antimicrobial, antiviral, anti-inflammatory, and immuno-booster  
93 activities.<sup>20</sup> Limited evidence, however, has been published in relation to effectiveness of such  
94 herbal remedies. In vitro studies in India demonstrated *Withania somnifera* (Ashwagandha),  
95 *Tinospora cordifolia* (Giloy), and *Ocimum sanctum* (Tulsi) linked to protease inhibition activities of  
96 SARS-CoV-2 virus.<sup>21</sup> In addition, the World Health Organization (WHO) has acknowledged the  
97 effectiveness of *Artemisia annua* (a medicinal plant- abundantly available in both India and  
98 Pakistan) as a potential pharmacotherapy research candidate against COVID-19.<sup>22, 23</sup>

99

## 100 **Middle East**

101 CAM is commonly used in the Middle East because it is linked to Islamic history with herbal  
102 treatments mentioned in Quran and is often known in the region as ‘Arabic’ or ‘Islamic’ medicine.  
103 CAM use is expected to grow at a compound annual growth rate of 22.8% from 2020 to 2027.<sup>24</sup>  
104 Since the pandemic reached the area CAM use is known to be common in the region.

105 In a recent study conducted in Saudi Arabia, over 1 in 5 (22.1%) of the 5258 survey respondents  
106 acknowledged their use of herbal products during the pandemic period because they believed  
107 that they are effective for the prevention of COVID-19.<sup>25</sup> Meditation or holy Quran recitation,  
108 cupping therapy (Hijama), acupuncture, massage, specific nutritional tonics, and herbs such as  
109 honey, dates, figs, peaches, garlic, olives, *Anthemis hyalina* (chamomile) and black cumin seeds  
110 are amongst the CAMs used for prevention and relief of symptoms include fatigue, loss of smell  
111 and breathing difficulties linked to COVID-19.<sup>26</sup> *Nigella sativa* when combined with grinded  
112 *Anthemis hyaline* and honey (TaibUVID was referred to prevention and treatment potential.<sup>27, 28</sup>  
113 Other herbal products described in the literature include garlic, onions, and ginger preparations.<sup>29</sup>

114

115 Several clinical trials on CAM have been registered in the Middle-east, notably, the phase II trial  
116 in Israel on the phytocannabinoid cannabidiol.<sup>30</sup> It is a non-psychotropic constituent of *Cannabis*  
117 *sativa* and possesses potent anti-inflammatory and immunosuppressive effects. These effects  
118 are mediated through the inhibition of proinflammatory cytokine release and stimulation of anti-  
119 inflammatory cytokine production.<sup>30</sup> A clinical trial in Egypt aims to evaluate the therapeutic  
120 potential of liquorice extract and *Boswellia serrata* gum.<sup>31</sup> These plants are reported to have anti-  
121 inflammatory, antiviral, antithrombotic, and immunomodulatory properties.<sup>32, 33</sup> A clinical trial in  
122 Iran aims to assess the effectiveness of colchicine combined with, herbal phenolic monoterpene  
123 fractions.<sup>34</sup>

124

### 125 **Africa**

126 The WHO estimates that more than 80% of the African populations rely on traditional medicine  
127 for their healthcare needs.<sup>35</sup> Traditional medicine has continued to gain acceptability in Africa  
128 due to its low cost, availability, and perceived low toxicity.<sup>36</sup> There is a lack of adequate data on  
129 the use of CAM during the COVID-19 pandemic in Africa. Recently the Madagascar Institute of  
130 Applied research linked the use of *Artemisia annua* (sweet wormwood) in COVID-19.<sup>37</sup> *Artemisia*  
131 *annua* is the source of antimalarial drug artemisinin. Potential widespread use has raised  
132 concerns amongst the scientific community in regards to malarial resistance to the drug.<sup>38</sup>  
133 Leaves of *Azadirachta indica*, *Mangifera indica*, *Eucalyptus globulus*, *Carica papaya*, *Psidium*  
134 *guajava*, *Citrus reticulata*, and *Musa paradisiaca* steam-inhaled and taken orally were shown in a  
135 recent study to be offering symptoms relief and restore physiological and psychological  
136 functions.<sup>39</sup> Zimbabwean government was reported to have authorised herbalists to treat patients  
137 with COVID-19 symptoms raising concerns among national public health experts.<sup>40</sup>

138

### 139 **South America**

140 Herbs and spices are very commonly used in Latin American countries. For example, in Brazil,  
141 the sales value of herbal drugs reached USD 187 million in 2019, a 3% annual growth compared  
142 to the previous year.<sup>41</sup> *Mikania glomerata* preparations have been known to be used in South  
143 America to treat respiratory illnesses such as cough and asthma. Bronchodilator action of the  
144 herb has been suggested.<sup>42, 43</sup> These are widely used and prescribed in Brazil, including their  
145 use in children.<sup>44</sup> Propolis produced by bees and commonly found in Brazil and exported to Asia  
146 including China, has been tipped to potentially interfere with host cell invasion by SARS-CoV-2.<sup>45</sup>

147

148 Indigenous communities in South America have also been reported to be using CAM during  
149 COVID-19. For example, herbal teas and root teas were reported to have been used by Dâw  
150 Indigenous communities in Brazil.<sup>46</sup> Anecdotal reports of patient experience suggested that they  
151 perceived the teas to have helped them cope with the symptoms.<sup>46</sup> A consortium of Latin-  
152 American and Caribbean Center has joined efforts in synthesising the evidence base in regards

153 to herbal medicines use in COVID-19.<sup>47</sup> Other herbs mentioned to have been used by  
154 Ecuadorian Amazon tribes include umu'co or cat's claw as antipyretic; wild ginger as a cough  
155 reliever, and cinchona bark as anti-inflammatory.<sup>48</sup>

156

### 157 **Europe and the North America**

158 CAM practices amongst communities in Europe and North America are diverse, reflecting the  
159 cultural diversities in these countries. In the US alone, it is estimated that over 20,000 different  
160 types of herbal products are available.<sup>49</sup> Herbal products regulations across Europe and North  
161 America are, however, varied. The US Food and Drug Administration (FDA) classifies herbal  
162 preparations as food supplements, and these herbal products do not require pre-marketing  
163 authorization from the FDA. However, such products should satisfy pre-marketing laws in  
164 Europe.<sup>50</sup> This includes adherence to criteria in regards to manufacturing and storage standards  
165 in Europe.

166

167 Anecdotal reports have suggested a surge in demand for TCM in the West during the initial  
168 phase of the pandemic leading to wholesale suppliers deciding to ration the supply to the  
169 retailers.<sup>51</sup> In a study conducted in Norway with CAM practitioners, relaxation techniques,  
170 prayers, ginger, and fish oils were some of the key practices they recommended to service users.  
171 Over 40% of the CAM practitioners in the study admitted that they would not refer COVID-19  
172 patients for treatment by a physician.<sup>52</sup> In the UK, herbs being sold as 'immunity boosters'  
173 against coronavirus were reported, which was considered against legal practice given the lack of  
174 evidence through clinical trials.<sup>53</sup>

175

176 Currently, limited research is being undertaken in the Europe and the North America to identify  
177 the effectiveness of CAMs including herbal medicines. Models of nano-fibre-based respiratory  
178 masks with herbal ingredients to minimise infection rates have been suggested.<sup>54</sup> Herbal  
179 products previously tipped to inactivate the Severe acute respiratory syndrome (SARS) virus and  
180 dengue fever, such as *Andrographis paniculate* are known to be amongst those being  
181 investigated.

182

### 183 **Discussion and conclusions**

184 Currently, the use of CAM in COVID-19 seems to be a common practice, globally. In particular, a  
185 range of herbal products across different geographical regions and continents are perceived by  
186 users to be effective in symptoms relief and/or treatment. Many governments have also formally  
187 or informally advocated or authorised the use of CAM in COVID-19, mainly based on their  
188 effectiveness in alleviating other respiratory symptoms or in some occasions on popular beliefs.  
189 CAM use in COVID-19 also reflected geographical, cultural, and religious practices.

190 Currently, limited research exists from human clinical trials in regard to the effectiveness of CAM  
191 in prevention, treatment, or symptom relief in COVID-19. In addition, gathering patient  
192 perspectives and experiences of CAM use in COVID-19 are imperative in informing future  
193 practices. Gathering data on common information queries received in community pharmacies,  
194 other healthcare settings and those described in internet forms will enable the development of  
195 evidence based information sources that can support effective patient counselling and  
196 communication practices.

197

198 At this time international clinical guidelines do not proactively encourage healthcare professionals  
199 to investigate patient use of CAM. It is known that up to 2/3<sup>rd</sup> of CAM users do not declare their  
200 CAM use with healthcare professionals.<sup>6</sup> COVID-19 patients, particularly with comorbidities and  
201 using medicines for long-term conditions, can benefit from evidence-based guidelines in regards  
202 to drug-herb or herb-disease interactions.

203

204 The COVID-19 pandemic has met international health systems with a low level of preparedness  
205 and emergency response. Healthcare professionals, including pharmacists, are likely to be  
206 sought advice and counselling regarding the use of CAM. Pharmacists have been traditionally  
207 offering services for self-care and common ailments including supply of non-prescription  
208 medicines.<sup>55-57</sup> It is imperative that counselling and communications practices by healthcare  
209 professionals, including pharmacists, in regards to CAM use are evidence based.

210 Phytochemicals have been integrated into the treatment of long-term health conditions such as  
211 cancer and gout. More extensive scientific evidence needs to be sought for their use in COVID-  
212 19.

213

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216

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220

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