

LETTER TO THE EDITOR**Traditional and complementary medicine during COVID-19 pandemic**

The recent corona virus disease-19 (COVID-19) pandemic has uniquely challenged medical research community worldwide due to absence of any vaccine or proven therapy. Repurposing of already available drugs is a prudent strategy for immediate management of those severely affected by the disease. To that end, clinical interventional studies are being conducted with multitude of drugs ranging from seemingly innocuous like zinc to potentially toxic drugs. Traditional and complementary medicine (T&CM) especially traditional

herbal medicines, however, find little mention in mainstream discourse of COVID-19 pandemic.

A comprehensive search of four prominent clinical trial registers (Table 1) finds scant representation of studies on T&CM in Clinicaltrials.gov and EU Clinical Trial Register (1.6%), while interventions like hydroxychloroquine and/or ivermectin feature prominently (17.8%). Clinical studies involving drugs of narrow therapeutic index like colchicine or oncological drugs/radiotherapy (4.8%) with

TABLE 1 Comparative number of interventional studies in various trial registries involving traditional/complementary medications compared to other specific treatments of interest

Clinical trial registry	Number of registered interventional studies ^a	Number of studies involving traditional/complementary medications ^b (%)	Number of studies on specific treatments of interest (%)	Example(s) of herbal remedies being evaluated and registered under various trial registries ^c
1. Clinicaltrials.gov	1,257	22 (1.7)	Hydroxychloroquine/ chloroquine: 202 (16.1) Ivermectin: 23 (1.8) Colchicine: 14 (1.1) Low dose radiotherapy: 12 (0.9) Oncological drugs ^d : 30 (2.4)	<i>Acacia Senegal (Senegalia senegal)</i> <i>Nigella sativa</i> <i>Caesalpinia spinosa</i> extract Acai palm (<i>Euterpe oleracea</i>)
2. EU clinical register	237	2 (0.8)	Hydroxychloroquine/ chloroquine: 38 (16.0) Ivermectin: 3 (1.3) Colchicine: 5 (2.1) Oncological drugs ^d : 11 (4.6)	—
3. Chinese clinical trial register	336	90 (26.8)	Hydroxychloroquine/ chloroquine: 25 (7.4) Oncological drugs ^d : 2 (0.6)	Liquorice (<i>Glycyrrhizae glabra</i>) Chinese skullcap (<i>Scutellaria baicalensis</i>) Honeysuckle (<i>Lonicera japonicae</i>) Huaier granule (<i>Tremetes robiniophila</i>) <i>Exocarpium citri grandis</i>
4. Clinical trial registry of India	28	21 (75)	Oncological drugs ^d : 1 (3.5)	Ashwagandha/Indian ginseng (<i>Withania somnifera</i>) Guduchi (<i>Tinospora cordifolia</i>)

Note: Studies on specific treatments on interest includes all studies where that particular intervention is part of either intervention or control arm.

^aAccessed on June 19, 2020. EU, European Union.

^bTraditional or complementary medications include any interventions out of modern medicine inclusive but not limited to traditional Chinese medicine, Ayurveda, Yoga, Unani, Siddha, Homeopathy, or other supplements (not including interventions with standard preparations of vitamins or zinc).

^cThe example list is only a representative (not exhaustive) list of various single herbal remedies registered for evaluation (not including concoctions of multiple herbal remedies) where details are available from respective trial registries. EU Clinical Trial Register does not have any study evaluating single herbal remedy formulation.

^dOncological drugs (number of studies) in COVID-19 include imatinib (8), nivolumab (5), pembrolizumab (1), selinexor (3), bevacizumab (5), acalabrutinib (4), ibrutinib (1), zanubrutinib (1), etoposide (1), melphalan (1), duvelisib (1), thalidomide (5), lenalidomide (1), methotrexate (1), sargramostim (4), and filgrastim (2).

significant known toxicities are already underway. The choice in most cases is based on thin base of evidence and often arbitrarily driven by popularity, familiarity, and/or availability.

In contrast, clinical trial registries of China and India show an overwhelming proportion of studies evaluating T&CM (30.5%) (Table 1). Traditional herbal remedies are popular and have strong sociopolitical patronage in these countries with national guidelines incorporating alternative medicines for management of COVID-19 (Ministry of AYUSH, India Advisory, 2020; World Health Organization, 2019). A recent systematic review have suggested that the integration of traditional Chinese medicine with "Western medicine" have improved cure rate with better symptom amelioration in COVID-19 (Liu et al., 2020).

As significant proportion of severe cases of COVID-19 is predominantly seen in "high risk" group (elderly people and those with pre-existing health conditions), (Zhou et al., 2020) safety profile should be of paramount importance while selecting molecules for repurposing and especially for prophylaxis. The toxicities of interventions evaluating chemotherapeutic drugs or drugs like Bruton's tyrosine kinase inhibitors with less than a decade experience are likely to be of more concern in the "high risk" group for COVID-19.


Medical science had limited success in developing broad-spectrum antivirals, especially for RNA viruses (Vigant, Santos, & Lee, 2015). Herbal medicines used in T&CM especially in traditional Chinese medicine or Ayurveda system of medicine in India are generally considered "safe" due to their widespread use over centuries. In general, assessing efficacy of traditional herbal remedies are often problematic due to inadequate and inconsistent methods being used across studies. Clinical research involving herbal remedies are ordinarily not conducted with similar rigor like other medical research. (Izzo, Hoon-Kim, Radhakrishnan, & Williamson, 2016). Therefore, the results from such studies should be extrapolated with caution. Randomized clinical trials involving herbal remedies conducted with sound and consistent methodology are imperative at this hour.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Sameer Bakhshi conceived the idea. Sameer Bakhshi and Shuvadeep Ganguly conducted review, literature search, and wrote the manuscript.

Shuvadeep Ganguly 

Sameer Bakhshi 

Department of Medical Oncology, Dr. B. R. Ambedkar Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India

Correspondence

Sameer Bakhshi, Department of Medical Oncology, Dr. B. R. Ambedkar Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi 110029, India.

Email: sambakh@hotmail.com

ORCID

Shuvadeep Ganguly  <https://orcid.org/0000-0002-7296-6088>

Sameer Bakhshi  <https://orcid.org/0000-0001-9367-4407>

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