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Discussion Kernel

Ayurveda: (W)here is the evidence

D.B. Anantha Narayana [a, *], Sharanbasappa Durg [b]

[a] Ayurvidye Trust, 1101/927, 1 F Main, 2nd Stage, Girinagar, Bangalore 560085, India
[b] H. No. 19-5-244/15, Ganachari Layout, Near Lumbini Nagar, Naubad, Bidar 585402, India

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ABSTRACT

It is common to hear a general statement that Ayurveda lacks scientific evidence. By scientific evidence, it is commonly referred to results of human clinical trials undertaken adoring those applied to pharmaceuticals, involving randomized controlled trials (RCT), either a placebo or active controlled. This paper explores the actual situation related to practice of Ayurveda, use of medicines, application of therapies, and the individual *dravyas* (ingredients). It gives few examples and availability of large body of scientific data in this area. The study, however, does not discuss the reasons and problems of conducting RCTs.

1. Background

Often, both in the lay press and at scientific meetings, statements that Ayurveda has no evidence are made. Here is a brief attempt to state the position.

The majority of healthcare in India centers on drugs and pharmaceuticals, devices and diagnostics. Such healthcare is delivered by doctors (MBBS or MD qualified) who obtain education and training in the contemporary biomedicine/surgery, differing from that the *vaidyas (practicing Ayurvedic clinician)* are taught. Attempts to supplement as add on or replace drugs and pharmaceuticals with Ayurvedic therapies/medicines have been going on for decades.

It is estimated that there are over 700,000 registered practicing *vaidyas* in India (with BAMS or MD Ayurveda qualification) for whom the question of where is the evidence should be redundant, due to their education and training in the practice of Ayurveda. A proportion of such *vaidyas* undergo an integrative medicine course which includes exposure to use of synthetic molecule based drugs in addition to Ayurveda. Some of the practicing *vaidyas* are also known to use modern medicine in their practice many times with a view to give quick relief in addition to using Ayurvedic methodologies and medicines. *Vaidyas* use preparations enshrined in either the *granthas* (authoritative texts) or proprietary Ayurvedic medicines (PAM) supplied by manufacturers or in Ayurvedic formulary or *Materia Medica* in their practice. There are 57 Ayurvedic books recognized as authoritative texts in the First Schedule to the Drugs and Cosmetics Act of India [1]. Preparations in these texts provide detailed recipes of the herbs/ingredients, levels of usage, process for manufacture, dose, indications and other relevant information. Such preparations manufactured as per the textual recipe are generally referred as Ayurvedic drugs as per the Act or in common parlance as classical preparations. The Drugs and Cosmetics Act permit combinations of ingredients listed in the *granthas*, but differing from the *grantha* recipes under a category referred as PAM. More than 80% of PAMs are having medicinal plants as their active ingredients. Medicinal plants based products are available globally, but all of them may not have been listed in the *granthas*. Medicinal plants based products are made using those plants which find a reference to the history of usage in *granthas* qualify as Ayurvedic medicines. However, those that do not find reference in the *granthas* qualify as herbal medicines. Such usage of either an Ayurvedic drug or a PAM as a supplement, add on or replace drugs and pharmaceuticals, needs adoption and acceptance by the doctors. This is where the aspect of evidence of efficacy and safety becomes pertinent.

The belief that the Ayurveda lacks evidence is incorrect. In this short exposition, we present different aspects of the evidence, its availability and the challenges involved. More specifically, the evidence demanded is for the Ayurvedic therapies (commonly referred to as massages) and Ayurvedic medicines. Randomized controlled trials (RCTs) involving human subjects/patients with a

* Corresponding author.
E-mail: drandba50@gmail.com
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group receiving either the treatment (medicine) or a placebo are considered necessary for such evidence. Do such evidences exist?

2. Ayurvedic treatment and products

2.1. Classical/Grantha products

A common *grantha* recipe, *Chyawanprash*, has been scientifically studied in India, Russia and other nations. *Chyawanprash*'s health benefits like protection from cold, cough, stress reduction, benefits to sportspersons, general well-being are reported. Chaukhamba publications' book (2007), "*Chyawanprash – from Vedic to Genomic Era*" (Fig. S1), documents these studies, and many of which are published in scientific journals [2]. Post publication of this book, a number of human studies has demonstrated this recipe's benefits on the immune system with regular consumption [3,4].

Further, classical product like *Arogyavardhini Vati* has been in use for centuries in treating cardiovascular disorders. A team of researchers from All India Institute of Medical Sciences (AIIMS) and Central Council for Research in Ayurvedic Sciences (CCRAS), New Delhi, investigated the efficacy and safety of Arjuna powder (5 g, twice daily for the first 3 weeks) and *Arogyavardhini Vati* (500 mg, twice daily for next 4 weeks) in 96 dyslipidemia patients; a total of 87 patients completed the study. Treatment with Arjuna powder and *Arogyavardhini Vati* significantly reduced total cholesterol, low-density lipoprotein, triglycerides, C-reactive protein, and blood glucose. The study also reported increase in high-density lipoprotein with no safety concerns in dyslipidemia patients [5].

The recipes documented in the *granthas* depict a long history of safe usage (HoSU). However, clinical trials on *grantha* recipes or traditional Ayurvedic treatment are far and few. Some of the reasons for this include the high costs involved and inability to own and protect the findings through patents. *Grantha* recipes are similar to generics in the pharmaceutical industry and can be made by anyone without claiming sole rights of production or marketing. This makes it unattractive for stake holders to invest in their scientific exploration as they lack deep pockets like the big pharma.

2.2. Ayurvedic treatment versus approved drug

Scientists at Arya Vaidya Pharmacy (AVP), Coimbatore, in their award winning research paper compared the safety and efficacy of complete Ayurvedic treatment against methotrexate – a synthetic approved drug in groups of patients with rheumatoid arthritis. Furst and co-workers including Ram Manohar of AVP undertook the study, and the results of this clinical trial are published in the Journal of Clinical Rheumatology (2011) [6]. This was a double-blind, randomized, controlled, pilot study comparing classic Ayurvedic medicine, methotrexate, and their combination in patients with rheumatoid arthritis. The clinical benefits, measured as per American College of Rheumatology Criteria, were observed in 86% of patients in methotrexate group, 100% in Ayurvedic medicine, and 82% in combination group. Differences in adverse events (AEs) among groups were not statistically significant, although the methotrexate group experienced more AEs. This study was partly funded by National Institutes of Health (NIH), USA. Currently, this study is further being extended to include larger number of patients in India. It is reported that a grant of Indian Rs. 27 million has been approved by the national funding agency for this study [7].

3. Proprietary Ayurvedic medicines

As stated earlier, Indian drug regulations also permit new combinations of Ayurvedic *dravyas* (herbs, minerals, ingredients with medicinal properties which are listed in the 57 authoritative texts, reserved by law as approved books) as PAMs [1]. Many Ayurvedic firms make these medicines, duly licensed by the authorities in State Drug Control or Directorate of Ayurveda. Such products are normally given a brand name or trade name. Many firms, including those in micro, small and medium enterprises (MSME) sector, get limited or focused human clinical trials (RCTs, double/single-blind or open-label) performed on at least a few of the products in their range and use the data to explain to *vaidyas* as well as doctors.

Many published studies are accessible through online search in electronic databases such as MEDLINE/PubMed and on the websites of many manufacturers. For example, The Himalaya Drug Company maintains the repository of research papers of their PAM products [8]. To list a few – Mentat™ [9], Liv.52™ [10], Koflet™ [11], Cystone™ [12], and Septilin™ [13].

Only some of these studies and findings get published in peer reviewed journals, the rest are quoted on literature of firm or the flip charts while explaining to doctors. Records of such claim support or evidence of efficacy and safety generated are not available in public domain. This puts severe limitation and causes challenges to trace evidence data. However, changing scenario in the last decades has seen publication of guidelines for human research and clinical studies including herbal and traditional medicines by Indian Council of Medical Research (ICMR) [14,15]. Mandatory need for registering any studies involving human subjects/patients on the Clinical Trial Registry (http://ctri.icmr.org.in/) of ICMR is helping to access the evidence online. Though such guidelines and requirements exist, however, many Ayurvedic MSME firms are still reluctant to and do not upload such studies data on the registry. It is also not known the proportion of registered clinical trials that upload the results at the end of the study completion and the proportion of clinical trials that get published with its findings in peer revived journals. This situation adds to the problem of availability of searchable data.

4. Evidence for *dravyas*

Evidence for a product is obviously dependent on the ingredients or *dravyas* (ingredients having specific properties resulting in pharmacological activity – from plant origin or metals and minerals or animal origin) that go into their composition. The last few decades have seen extensive scientific data generation on Ayurvedic herbs in research journals globally. ICMR is one such national body which not only funded such research, but also brought out high quality scientific publications. The 22nd volume of Reviews on Indian medicinal plants (2020) covering plants whose name begins with "Qui" provides a compilation of comprehensive scientific data on medicinal plants [16]. ICMR has published 19 volumes of Quality Standards of Indian medicinal plants covering more than 600 plants [17], Fig. S2a. ICMR's recent output is 3 volumes of Safety Reviews on 50 plants [18], Fig. S2b. The Government of India, through other funding agencies mainly Department of Biotechnology (DBT), Ministry of Ayurveda, Unani, Siddha and Homeopathy (AYUSH), National Medicinal Plants Board (NMPB), and Council of Scientific and Industrial Research (CSIR), has funded such research on plants for past decades.

Indian Pharmacopoeia provides over 160 monographs for herbs, extracts and products [19]. United States Pharmacopoeia, and its Formulary includes monographs on over 350 plants, many of which are in Ayurveda [20]. Ayurvedic Pharmacopoeia provides quality specifications for over 650 plants. Mark Blumenthal, a scientist specializing on herbs in the US has published a series titled "HerbClip™", available on American Botanical Council website. HerbClip™ provides thousands of insightful summaries and critiques of clinical studies and related botanical science publications

Fig. 1. Schematic representation of visible and non-visible Ayurvedic evidence.

covering research, regulation, marketing and responsible use of medicinal plants [21]. HerbClip™ allows advanced search to access the original article back to 1995 by number, title, keyword, text, or citation (journal, author, title) of the publication. Numerous HerbClip™ reviews are available freely in public domain, whereas access to the entire database is reserved for members at the academic level and higher. The issues available on HerbClip™ Online are from 1995 onward covering 074 to 638 issues.

It is estimated that over 2300 scientific research papers are published (PubMed) as of date (21 July, 2020) giving data covering on Turmeric (*Curcuma longa*), the *mangala* (considered auspicious, with multiple benefits so much so such ingredients are used as offering to the almighty and human) *dravya* of India alone. The evidence on turmeric, its medicinal properties, and health benefits are so strong culminating in popular consumption of the golden milk abroad, a practice that our grandmothers told us to do. Milk with added turmeric powder or extract is sold next to Cappuccinos, as Curcuma Latte to protect and prevent from infection and provide immunity benefits.

There are many scientific books covering research in Ayurveda and Ayurvedic herbs. Post Graduate Centre for Research in Ayurveda, Jamnagar, has brought out a CD documenting the research published in MD and PhD thesis in Ayurveda across the nation from somewhere in 1945 till date, and is titled as “Researches in Ayurveda” [22]. In 1997, “Researches in Ayurveda” was first published with almost 4100 theses titles. After initial positive response from research scholars across the country, a second edition (2005) was launched in well classified form with update of research works of about 7600 theses titles of postgraduate and PhD works conducted at 50 Ayurveda postgraduate institutes. Following this, a third edition was attempted to keep the information up-to-date and the content was brought online. The current website edition is presented in easy, searchable form to the postgraduate scholars of Ayurveda, which contains 20,000 titles from more than 60 postgraduate institutes of Ayurveda. The keywords can be searched in the ‘Search Form’ and output will be displayed department wise.

5. What about therapies?

The evidence on effectiveness of Ayurveda is not limited to products, but also extends to therapies. There are more than 30 therapies categorized under modalities such as *Panchakarma* (purification procedures for the body), *Abhyangam* (whole body oleation), and *Shirodhara* (pouring oil or liquids in a steady stream on the forehead with slight massage on head for around 45 min). The health benefits of *Abhyangam* have been documented and published in scientific journals [23,24]. Beyond India, scientists in Japan have studied the neurological benefits of *Shirodhara* several years ago [25]. This published study describes the potential mechanism and outcomes of *Shirodhara*. Similar outcomes are also seen in other published studies on *Shirodhara* [26,27]. *Jaluka*, another valuable therapy, involves use of leeches to suck the venous blood from varicose veins and provide effective relief to patients. This therapy is now approved by the US Food and Drug Admiration (FDA) with operating procedures and protocols for breeding and culturing right type of leaches etc. The US FDA general and plastic surgery review panel defined this as the device is a medicinal leech (*hirudo medicinalis*) belonging to the annelida worm classification. The animal is a bloodsucking aquatic animal living in fresh water. The device should be indicated as "an adjunct to the graft tissue healing when problems of venous congestion may delay healing, or to overcome the problem of venous congestion by creating prolonged localized bleeding” [28].

Kshara sutra (medicated thread tying technique for treatment of anal fistula) has been accepted by surgeons, and many of them are using this method as an alternative to surgery. *K. sutra* provides

relief with much better outcomes, i.e., less pain and reduced need for hospitalization [29]. *K. sutra* has also been extensively studied in Japan and practiced in different hospitals in Japan [30–32]. There is thus a large body of scientific data.

For today's tech savvy persons, who majorly access information through the internet, unfortunately such evidence is not easily accessible through online search. This makes them to believe that if online search yields very little or no data - evidence does not exist. However, inability to search other forms of publications like thesis/books/monographs/*granthas* etc., makes them to believe absence of evidence (Fig. 1).

It is learnt that ICMR is working to make all the data in their publications digitized and provide them for online search access. Many databases are not free and need to be subscribed. *Granthas* and books that provide a documented history of safe and effective use are more difficult to access through an online search, and particularly as many of them are in the Sanskrit language. *Charaka Samhita* (the first treatise on Ayurvedic healthcare science, 1500 BC) and a few *granthas* published later, have been digitized by private organizations [33]. Scientific data on over 600 commonly used Indian medicinal plants exists in these publications. On many plants, one can see results of human clinical studies. Of course, gaps in the data may still exist for a particular effect or benefits that one is looking for. India is one of the very few nations possessing such documented traditional knowledge and evidence of history of use. *Agada tantra*, the important chapter in Ayurveda, describes safety and toxicology aspects in Ayurveda. *Vaidyas* quoting these say "extensive observations and studies were needed before any *dravya* could find a place in the recipes of *granthas*, as much as 50 years with knowledge of the safety profiles".

There is a saying in scientific enquiry, quote 'that the absence of evidence is not the evidence of absence' unquote. To quote Dr. Mashelakar – an internationally known scientist and formerly Director General of CSIR, quote "parachutes work only when they are open" unquote.

Generalization that evidence for Ayurveda is lacking needs a rethink.

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Conflict of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jaim.2020.07.001.

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