Surgeon Senjee Pulney Andy's trials in treating smallpox using leaves of *Azadirachta indica* in southern India in the 1860s

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Indian people hold *Azadirachta indica* (Rutales: Meliaceae) (*nimba*, Sanskrit), a native tree, in high veneration. Its cultural connections with the people of the Indian subcontinent are complex and intense[1]. References to its use exist in *Çaraka*, *Suśruta* and *Brihat Samhitã*-s – the ancient Sanskrit medical treatises[2,3]. Today we know of 300 different chemical substances from *A. indica* (O. Koul, pers. commun.), a majority of which are limonoids in seeds. Several research articles referring to the relevance of these limonoids to humans exist[4,5]. Azadirchtin, a tetranortriterpenoid, is an environmentally friendly active principle used as a 'pesticide' to manage pestiferous arthropods and pathogenic fungi[6,7], thanks to a casual observation of Heinrich Schmuterer on *Schistocerca gregaria* (Insecta: Orthoptera: Acrididae), while working on the locust plague in northern Africa[8] in 1959. A comprehensive summary of diverse medicinal capabilities of *A. indica* is available in Biswas *et al.*[9]. Several commercially available cosmetic products based on *A. indica* compounds (e.g. *Margo* bath soap (note 1)) are well known[8]. People of the Indian subcontinent consider *A. indica* a 'divine' tree that protects them from illnesses such as smallpox, chicken pox, measles, mumps, and even herpes, which we know today are caused by viruses (Figure 1).

Figure 1. 'Leaves of *A. indica* relieve the discomfort of smallpox.' (Aikman, L., *Nature's Healing Arts: From Folkmedicine to Modern Drugs,* The National Geographic Society, Washington, DC, 1977, p. 132.)

In such a context of cultural and economic relevance of *A. indica*, we found a short article referring to his trials using leaves of *A. indica* in treating smallpox by Madras surgeon Senjee Pulney Andy[10] (hereafter PA), when he was the Superintendent of Vaccination in Travancore (note 2) in the 1860s. This article appealed to us because only in 1892, two-and-a-half decades later, we ever knew of viruses, with Dmitri Ivanovski (1864–1920) demonstrating the transmission of tobacco-mosaic virus, confirmed by Martinus Beijerinck (1851–1931) in 1898 (ref. 11).

Senjee Pulney Andy

PA was born in Ŧiruchirapalli in 1831. After his early education in the Madras Christian College and qualifying for MBCM from the Madras Medical College (note 3), he qualified for MD from the University of St Andrews (Fife, Scotland) in 1860. After acquiring Membership of the Royal College of Surgeons of England in 1861 (note 4), he returned to Madras in 1862 (Figure 2). The Government of Madras appointed him as the Superintendent of Vaccination in Calicut, Malabar, because the residents of Malabar suffered pock diseases extensively[12]. Records indicate that PA published his scientific work in professional journals. A detailed note on the life and scientific work of PA is published elsewhere[13]. PA was the first Indian to qualify for an overseas medical degree. Anandibai Joshi from Poona qualified for MD in Pennsylvania in 1886; Kadambini Ganguly *née* Bose from Calcutta qualified for LRCP (Edinburgh) and LRCS (Glasgow) in 1892.

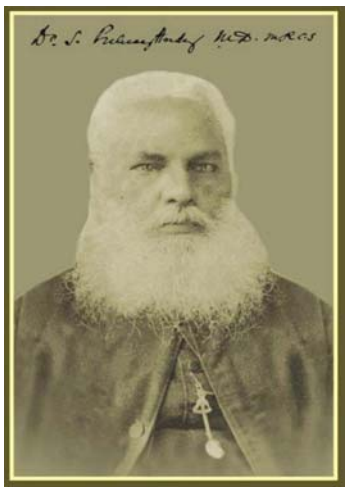

Figure 2. Senjee Pulney Andy. (Courtesy: Ravi Senji, Madras.)

Andy's trials using *A. indica* leaves in treating smallpox

Details of PA's trials on smallpox treatment using leaves of *A. indica* are summarized below[10]:

(1) Trials were made in Alwaye (10°07′N; 76°21′E) on the banks of the Périyãr on six patients suffering from smallpox in the hot months (note 5).

(2) Why did he choose to use margosa leaves as the medication: 'In the absence of other drugs , I took the opportunity of prescribing the Margosa ...'.

(3) He prescribed that the

- tender leaves of *A. indica*
- leaves with stem of *Artemisia austriaca* (Asterales: Asteraceae)
- root of *Glycyrrhiza glabra* (Fabales: Fabaceae)

be mixed and ground with a few drops of water and the ground mass to be divided into pills of five grains (note 6) each.

(4) He provides a short description of the illness among the patients he treated: '... all were of confluent form in adults. Two of them were on the 4th, three of them on the 7th and the 8th, and the other on the 15th day of the disease'.

(5) Except the last one who died 'of exhaustion' the same day, all others recovered.

(6) He visited Alwaye in November again (same year?) and could help eight more people. He seems to have pre-

scribed the same medication (as above) to these people also; except one aged 50 (who died because of malignant type of smallpox), the rest recovered.

(7) He remarks as follows: 'As far as I had an opportunity of testing the drug in these 14 cases, it appeared to be beneficial, when administered during the premonitory and progressive stage of the disease and to be of little or no use after the eruption had passed the stage of maturation. It seems to decrease the severity of fever, facilitate in throwing out the eruption freely, and alleviate all other sufferings usually experienced in this disease. In fact, the patient expresses himself as passing through several stages of the disease with comparative ease, without much pain or uneasiness.'

PA also suggests: 'In places where fresh plants cannot be had, I would suggest the use of dried tender leaves of Margosa either in the form of infusion or decoction, with the other ingredients in the proportion of a drachm each to a pint of water. The dose for an adult was one ounce of the decoction twice or thrice a day (note 6).'

Remarks

At the start of his article, PA refers to *A. indica* as a venerated symbol in honour of the female deity *Mariatha* in rural southern India. He derives the prefix *Mari* from *marakka* (Sanskrit), which means death. He explains[10]:

> '… it is probable that the ancient Hindus might have defied the destructive tendency of Nature, and classed her amongst their Mythological Deities.'

PA then refers to *vasuri*, a commonly used term for smallpox in southern India even today. He derives *vasuri* from *masurika* (Sanskrit), which means gram (note 7), the disease manifesting as gram-like eruptions. Whereas the derivation of *vasuri* from *masurika* is acceptable, derivation of *Mari* from *marakka* is not. What PA writes as *Mari* should be read as *Mãri*. Although both *mari* and *mãri* exist in Tamil vocabulary, they mean differently. *Mãri* means rain, whereas *mari* means death. The extended intonation of *a* – to be read as *ã* – makes the difference. Therefore, what Andy describes as the female deity *Mariatha*, should be read as *Mãriãthã*, where *ãthã* is mother and *mãri* is rain: the Mother, who is as benevolent as the rain.

PA suggests that he was 'inspired' to use the leaves of *A. indica* in his Travancore trials based on previous work in treating smallpox using *Saracenia purpurea* (note 8) and *Nepenthes distillatoria* (note 8), although he does not cite any references in support of this claim. We could track down several articles written by medical practitioners using *S. purpurea* in treating smallpox[14–16]. Chalmers-Miles[14], an Assistant Surgeon with the Royal Artillery in North America then, indicates that in the late 1800s, the Micmac Indians of Nova Scotia, Canada used a plant-based remedy for smallpox:

> 'an old squaw going amongst them, and treating the cases with (a botanical) infusion … was so successful as to cure every case.'

The 'botanical infusion' was identified by Chalmers-Miles as from the carnivorous plant *S. purpurea*. Renshaw[16] from Altrincham (Trafford, Manchester, UK) reports treating five patients with a decoction of *S. purpurea* who, he claims, were cured of the illness, and concurs with the medical report of Chalmers-Miles[14]. We could not track down any professional journal papers trialling *N. distillatoria* in the treatment of smallpox, although a few unverifiable Internet sites exist referring to its use in the treatment of smallpox in Homeopathy.

In contemporary pharmacology, various compounds extracted from different parts of *A. indica* are indicated to possess antimicrobial properties. Extracts of leaves, especially, are considered useful in treating several skin problems, e.g. dermatitis, eczema, acne[17], probably due to many sulphur compounds (O. Koul, pers. commun.). In principle, *A. indica* extracts strengthen the immune system[18]. In high likelihood, the strength of *A. indica* is the effect it bears on skin. Preparations from leaves or the oil are used as an antiseptic. In the context that it can be used in treating skin disorders, and its capability in strengthening the immune system, *A. indica* compounds act countering viral disorders such as smallpox, chicken pox and warts, particularly when applied to the skin. Its efficacy, in part, is due to its ability to inhibit viruses from multiplying and spreading[19]. The bitter principles of *A. indica*, viz. nimbin, nimbinin, nimbidin, and the terpenoid azadirachtin have been verified for their antiviral capabilities. *In vitro* antiviral activity of aqueous *A. indica* leaf extract, assessed in cloned cells of the larvae of *Aedes albopictus* (Insecta: Diptera: Culicidae) using virus-inhibition assay showed inhibition of the virus in a dose-dependent manner[20]. Whereas the precise mode of action of *A. indica* components against viruses has not been established, indications are that they interfere with viral reproduction reducing their impact. For instance, the effect of azadirachtin on the replication of dengue virus type-2 is known[21]. Components of *A. indica* enhance macrophage response in the human body, thus stimulating the lymphocytic system improving white blood cell production and their numbers[22].

Why PA added the leaf and root materials of *Artemisia austriaca* and *G. glabra* respectively, to the ground leaves of *A. indica* is unclear. Were they added to enhance the efficacy of *A. indica*? However, contemporary phytochemistry sheds light on the possible role of *Artemisia* in decoctions prescribed by PA for patients of smallpox in Alwaye. For example, Sinico *et al.*[23] demonstrate in their antiviral assays that the liposomal incorporation of the essential oil of *Artemisia arborescens* enhanced its *in vitro* antiherpetic activity. Similarly, roots of *G. glabra* are also being currently shown to possess antiviral properties; the triterpinoid saponin glycyrrhizin, the most prominent active compound in *G. glabra* roots, has been shown to prevent virus binding with host tissues[24].

What is obvious today is that the plants chosen and used by PA in treating patients of smallpox possess some level of anti-viral properties; but what is not clear is whether those plants were particularly effective against pock viruses, since the contemporary pharmacology demonstrates their efficacy against either herpes zoster or other skin manifestations because of immune deficiency induced by viruses.

Notes

1. Margo bath soap, launched by Calcutta Chemical Company in 1920, now a Henkel–SPIC product.
2. Travancore was a princely state in southern India, outside the jurisdiction of the Madras Presidency during colony days.

Maharājā Āyilyam Ŧirunāl Rāma Varmā ruled Travancore State from Ŧiruanantapuramin the 1860s. Today this is a part of Kerala. How PA went into Travancore-government service from that of Madras Presidency is unclear.

3. MBCM (*Medicinae Baccalaureus et Baccalaureus Chirurgiae*), the 19th century equivalent of modern MBBS, was offered in the Madras Medical College from 1857. During 1850–1857, the title 'Graduate of Madras Medical College' was awarded[25].
4. The *Calendar of the Royal College of Surgeons of England* (1 August 1916, p. 155, Taylor & Francis, London) lists PA as a Member of the Royal College of Surgeons of England with the year of admission into the College marked 1861.
5. Possibly May–July, year not indicated.
6. Apothecary's measures: 1 grain = 64.78 mg; 1 drachm = 1771.85 mg; 1 pint = 473 ml; 1 ounce = 29.57 ml.
7. 'Gram' means 'lentil-like'; recall 'horse gram' (*Macrotyloma uniflorum*, Fabales: Fabaceae).
8. *Sarracenia purpurea*, Sarraceniaceae; *Nepenthes distillatoria*, Nepenthaceae.

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