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Amoebic Dysentery and Introduction of Emetine Source *Carapichea ipecacuanha* into Indian Subcontinent

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Abstract

The South-American herb *Carapichea ipecacuanha* was feverishly sought after in Europe, since it gained a new popularity as a material useful in treating dysentery, especially after the treatment of Dauphin Louis — the eldest son of Louis XIV of France — by Johann Schweitzer (Jean Helvétius) in Paris in 1686. With the isolation and characterization of emetine from *C. ipecacuanha* roots by Magendie and Pelletier in France in 1817 and with its increasing relevance in managing amoebic dysentery, Britain, among the other European nations, was keen to introduce this plant for cultivation in India. The present article chronicles the efforts made by the British Government to bring and install *C. ipecacuanha* at a commercial scale in India — in Calcutta and neighbourhood and the Nilgiris and neighbourhood — in the later decades of 19th century. Because of the value attributed to *C. ipecacuanha* in managing amoebic dysentery — a public-health problem of high concern in the 19th century — this article also features the pioneering and fascinating trials made by senior surgeons, such as Leonard Rogers of the Calcutta Medical College in 1910s.

Key words: British Government, Calcutta, *Entamoeba histolytica*, Nilgiris, ipecac farms, Public health, South America

1. Introduction

Dysentery was, and continues to be (Peterson *et al.* 2011), one strong force to battle with in a tropical country such as India. During World War I, for example, 4-7% of the total number of in-patients in military hospitals in North Africa suffered acute dysentery caused by *Entamoeba histolytica* (Protozoa: Amoebida: Entamoebidae), many resulting in fatalities[1] (Woodcock 1917). The Sanitary Commissioner's report for 1905 (Government of India 1906, p. 74) indicates 0.027% and 0.018% mortality due to dysentery (amoebic?) among army personnel and prison inmates for 1904 and 1905, respectively.

James Annesley's (1780-1847, Madras Army Medical Service) *Researches into the Causes, Nature and Treatment of the More Prevalent Diseases of India and of Warm Climates Generally* (1828) is one early volume that refers to both intestinal and hepatic amoebiasis at a high level of accuracy (Cox 2002). Much of the medical literature of this period refers to the undesirable consequences caused by amoebic dysentery, in

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[1] Friedrich Lösch (also known as Fedor Lösch) of St. Petersburg isolated Protozoa from human faeces in 1875, and named them as *Amoeba coli.* Fritz Schaudinn renamed this as *Entamoeba histolytica* in 1903, because he found that the protozoan induces tissue lysis.

most instances leading to death of people because of rapid dehydration. Colostomy was one considered treatment strategy (Sullivan, 1900), although today it is not, thanks to the discovery of nitroimidazole family of antibiotics, *e.g.*, metronidazole and tinidazole, in the 1950s (Nakamura, 1955). By 1925, close to 10% of the European and American population harboured *E. histolytica* cysts (Brug, 1925). Until the 1960s, to treat patients suffering amoebic dysentery, surgeons used root extracts of *Carapichea ipecacuanha* as oral administrations of the active principle — emetine. Emetine was chemically characterized by Magendie and Pelletier in France in 1817. Botanists referred *C. ipecacuanha* variously as *Psychotria emetica, P. ipecacuanha, Callicocca ipecacuanha*, *Cephaëlis ipecacuanha,* and *Urogoga ipecacuanha*, whereas medical personnel referred to this plant as either 'ipecacuanha' or 'ipecac'.

Surgeons in India used *C. ipecacuanha* to treat amoebic dysentery with greater enthusiasm than their contemporaries in other tropical countries in the 19th century (see Douglas, 1913). Edward Scott Docker of the Indian Army Medical Service, while stationed in Mauritius, first tried 'large doses' of ipecacuanha[2] to treat dysentery in 1858 and succeeded in reducing patient mortality from 18 to 2% (1858). Consequently, surgeons in India used large doses of *C. ipecacuanha* root extracts. Surgeon William Cornish of Madras Medical Service, for example, reports (1861) the beneficial effects of using large doses of ipecacuanha based on personal trials; he also summarizes the positive experiences of several Madras surgeons on the efficacy of this root material. A similar extensive study evaluating the usefulness of large doses of ipecacuanha by Joseph Ewart of the Bengal Medical Service appears to have been published in the *Indian Annals of Medical Science* (1863), wherein the science of action of ipecacuanha is indicated to be explained convincingly (quoted from Fayrer, 1881; p. 64):

> 'In large doses it (*sic*. ipecacuanha) stops inflammatory action, augments the alvine secretions from œsophagus to rectum, increases the flow of bile and pancreatic juice, purges without irritating, lessens peristaltic action, produces rest, restrains tormina and tenesmus, promotes diaphoresis, restores the balance of portal circulation, is a direct sedative of cardiac action; acts on the glands of the stomach, and duodenum, pancreas, liver and the small, intestine, and on the glands of large intestine.'

The Docker trial encouraged surgeons around the world to follow his method in dysentery management. American surgeons, in particular, followed this practice (Thompson, 1913). However in the last decade of the 19th century, use of ipecacuanha in treating amoebic dysentery and hepatitis fell out of favour among medical practitioners with the emergence of safe, chlorinated water supply as a better and easier public-health management option, thanks to American surgeons John Leal and Alexander Cruickshank (Baker, 1981).

Edward B. Vedder, US Army Medical Corps, stationed in Manila, the Philippines, made a trailblazing experimental study evaluating the efficacy of emetine in treating amoebic dysentery in 1910. Vedder tested the potency of emetine in killing amoebae in *in-vitro* trials and reported his results at a Manila-Medical Society meeting in 1911. Leonard Rogers of the Calcutta Medical College perfected a method to inject emetine hypodermically[3]. Rogers (1912) reports his successful clinical trials made on three patients: one suffering acute haemorrhagic amoebic

[2] 'Large doses' meant 60-90 grains of pharmacopeia-standard ipecacuanha, administered to patients, 2—3 times a day. 1 grain= 60 mg.

dysentery, the second severe chronic amoebic dysentery for 3½ years, and the third acute hepatitis. This 'discovery' of injecting emetine solution hypodermically revolutionized amoebic-dysentery management. Hypodermic administration of emetine also cured liver abscess, a common consequence of acute amoebic dysentery.

Roots of *C. ipecacuanha* were brought by Willem Piso from Brazil to Europe in 1649. Piso highlighted the importance of *C. ipecacuanha* in *Historia Naturalis Brasiliae* (1648) — probably, the oldest, formal documentation of *C. ipecacuanha* use. However this material was scarcely used by the Europeans until the early decades of the 1700s. In 1686, a French merchant, Grenier, brought 150 lbs (68 kg) of dry *C. ipecacuanha* roots from Spain to France. This material was used by Johann Schweitzer (Jean Helvétius[4]), who first used it in treating dysentery suffered by Dauphin Louis, the eldest son of Louis XIV and Crown Prince of France (Thomson, 1826). The use of this root as an emetic (one that induces vomit) was found by Gottfried Wilhelm Leibniz of Hannover (1696), who is better remembered for a key methodological paradigm in research. Leibniz uses the words '… *magnis successibus comprobato*' (attested with great success) in the title of his monograph, which demonstrates that he 'tested' the efficacy of its roots, on himself, since he experienced *ein kleines Grimmen* (a small gripping pain) in 1695, as though he had consumed a purgative (Smith, 2011).

2. Nomenclature and Biology of and Active Principles in *Carapichea ipecacuanha*

Although Piso had referred to *C. ipecacuanha* (not known so at this time) in *Historia Naturalis Brasiliae* (1648), Piso's notes on this plant were inadequate for it to be formally named biologically. Based on the material supplied by Joseph Celestine Mutis, a physician to the then Viceroy of New Granada (*Nueva Granada*, parts of modern Columbia, 12°07'N, 61°40'W) (Smith, 1821), Linnaeus described this material as *Psychotria emetica* in *Supplementum Plantarum Systematis Vegetabilium* (1781). Félix Avellar Brotero of the University of Coimbra (Portugal) described this plant as *Callicocca ipecacuanha* in 1802 (Fig. 1). The same description occurs also in Bernardino Gomes's monograph *Memoria sobre á ipécacuanha fusca do Brasil, ou Cipó das nossas boticas* (*Memoir on ipecacuanha of Brazil or Cipó for our pharmacies*) dated 1801 (pages 27–30) signed by Brotero as 'Félix Avellar Broterus'. Christiaan Persoon, remembered today for his work on fungi, named this plant as *Cephaëlis ipecacuanha* in 1805 (p. 203). These are a few examples to illustrate how a range of binomials were created for this plant over time. For a crisp summary of the history of nomenclature of *C. ipecacuanha*, see Lloyd (1921, 168-169).

Nadkarni's *Indian Materia Medica* [*IMM*] (1996) includes a table, details mostly drawn from Chopra (1933), that compares the levels of (i) total alkaloids and (ii) emetine (expressed as

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3 Hypodermic needles came into use in the second half of the 1800s. Syringes came into use after the invention of hollow needles. Alexander Wood (Scotland) and Charles Pravaz (France) independently contributed to this development in 1853. Hypodermic needles enabled injection of medications into human bodies. Early syringes consisted of glass barrels with holding parts made of silver. Silver needles were used and re-used after sterilization. Unlike modern syringes that have plungers, early syringes worked by turning a screw at the top to inject the liquid. Syringes with plungers, made fully of frosted glass, came into use by the 1900s [http://www. sciencemuseum. org.uk/broughttolife/objects/display?id=5099].

4 Johann Friedrich Schweitzer (1625-1709) of Swiss-German roots changed his name as 'Jean Fridericus Helvétius' after moving into Paris from the Netherlands. Note the Latin name of Switzerland ('Schweiz'- German) is 'Helvetia' (or '*Confœderatio Helvetica*'). Some references indicate Johann Schweitzer a trained medical doctor; a few others label him a 'quack'.

Fig. 1. *Carapichea ipaecacuanha* labelled *Callicocca ipecacuanha* in Brotero (1802). For explanation of numbers and letters of alphabets used, refer to the original.artwork by J. Quinn, 1800

percentage) in *C. ipecacuanha* roots of Brazilian, Columbian, and Indian distribution. The greatest level of emetine is reported in plants of Indian occurrence (1.39), although the total-alkaloid levels were far less in Indian populations of *C. ipecacuanha*. The *IMM* lists *Cryptocoryne spiralis* (Alismatales: Araceae), *Tylophora asthmatica, Asclepias curassavica, Anodendron paniculatum, Calotropis gigantea, Sarcostemma glaucum* (Gentianales: Apocynaceae: Asclepiadoideae), *Gillenia stipulacea* (Rosales: Rosaceae), *Euphorbia ipecacuanhae* (Malphigiales: Euphorbiaceae), and *Boerhaavia hirsuta* (Caryophyllales: Nyctaginaceae) as substitutes for *C. ipecacuanha*, mainly because of their emetic property, although none of these includes either emetine or cephaëline found in *C. ipecacuanha*. Chopra and Chopra (1955, pp. 165-166) offer a bibliography on the biology, chemistry, and pharmacology of *C. ipecacuanha*.

H. Kunz provided the molecular structure of emetine ($C_{30}H_{40}N_2O_5$) (Fig. 2) in 1887 (Simonson, 1890), which remains valid today (Craig and Stitzel, 2004). Roots of *C. ipecacuanha* include the greatest level of emetine, its stems and leaves including less, and the seeds none (Hooper[5],

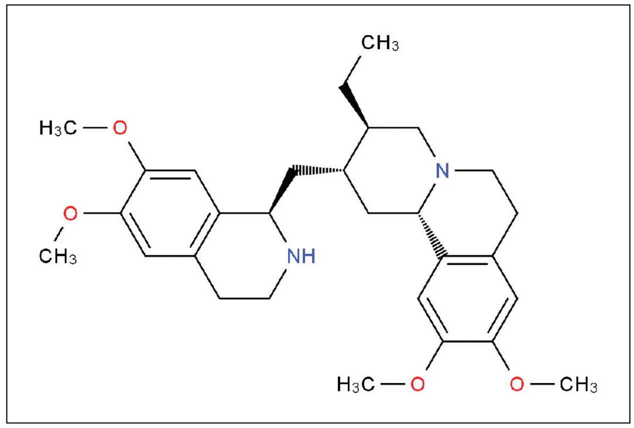

Fig. 2. Emetine [Molecular formula —$C_{29}H_{40}N_2O_4$; molecular mass— 480.6389]

(Source:http://en.chembase.cn/molecule 167981. html # 2d_img)

1892). Flückiger obtained emetine hydrochlorate in crystalline form (1891), which gained significant use in medicine. British chemists B. H. Paul and A. J. Cownley isolated and characterized the other alkaloid cephaëline from *C. ipecacuanha* roots in 1894 (Fig. 3).

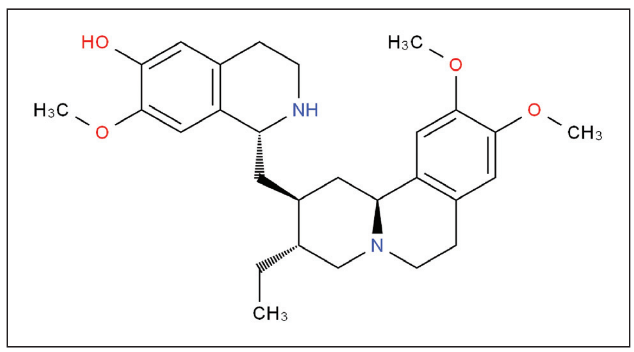

Fig. 3. Cephaëline [Molecular formula — $C_{28}H38N_2O_4$; molecular mass — 466.61232]

(Source: http://en.chembase.cn/substance-378895.html)

Trials determining the specific roles of emetine and cephaëline indicated that emetine was a 'good' expectorant, whereas cephaëline was not; cephaëline was superior as an emetic (Anonymous, 1896). Biosynthesis of emetine and cephaëline (*e.g.*, Asano *et al.,* 2002) and the

[5] David Hooper, a British Chemist, was the Quinologist (Chemist) attached to the Madras Cinchona Plantations in the Nilgiris in the 1890s.

ecology of variations in alkaloid production in *C. ipecacuanha* populations in diverse geographical regions (Garcia *et al.,* 2005) are being pursued currently. For brief, comprehensive notes on the chemistry of *C. ipecacuanha*, its indications and contraindications in medical applications, making ipecac preparations as teas, regulatory statutes in various countries, and a bibliography on its uses as an emetic agent and in treating amoebiosis the reader may consult Wichtl (2004, pp. 309-311) (Fig. 4). The progression of interest in *C. ipecacuanha* globally and its relevance in treating amoebic dysentery are chronicled in Lee (2008). One other relevance of ipecacuanha was in *Pulvis Doveri* (Dover's powder, *Pulvis Ipecacuanhae et Opii*) developed by Thomas Dover (16601742), which included opium and morphine added to ipecacuanha (Morton, 1968). Dover's powder was rated a valuable diaphoretic and analgesic, and was used in treating fevers and pains both by English-medical and Homeopathy practitioners (Gibson, 1965).

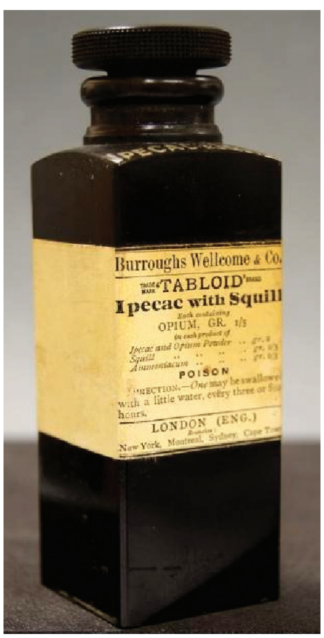

Fig. 4. Ipecacuanha—Squill compound in a gutta-percha container, 19th century

(Source:http://collectionsonline.nmsi.ac.uk/browser. php ?m=objects)

Carapichea ipecacuanha is cultivated presently in various tropical nations of the world: India and Malaysia in the East, and Nicaragua and Panama in the West. 'Rio' (or 'Matto Grosso'), 'Bahia', 'Minas', 'Johore', 'Cartigenea', and 'Nicaragua' are the known cultivars of South-American populations of *C. ipecacuanha*, recognized based on starch-grain index (Duke and deCellier, 1993). The molecular genetics of *C. ipecacuanha* populations sampled from the Atlantic range (eastern edges of Brazil) and the Amazonian range (the western edges) of Brazil indicate a high level of variability in populations of *C. ipecacuanha* and the breadth of genetic flexibility (de Oliveira *et al.*, 2010). Similar studies on Indian populations of *C. ipecacuanha* are lacking. Probably the Indian population of *C. ipecacuanha* too has evolved with local soil and climatic conditions over the last 125 years of introduction from Brazil, either to the better or to the worse, measured in terms of alkaloid production. India produced 20 metric tons of dry roots of *C. ipecacuanha* in 1978 (Sundaresh, 1982).

3. Introduction into and Cultivation of *Carapichea Ipecacuanha* in India

Interest on introducing 'useful' plants into India has been brewing from the early decades of 19th century. John Forbes Royle (author of *Illustrations of the botany and other branches of the natural history of the Himalayan Mountains, and the flora of Cashmere*, 1835—1839) in a memorandum dated 13 April 1836 submitted to George Eden, the First Earl of Auckland, Governor-General of India (1836—1842) (Royle, 1839) says (p. 37):

> 'The introduction of plants both useful and ornamental into India from other countries, though carried to some extent, has not yet been effected to the degree which is advisable, considering the benefit to be derived, and the great probability of success, if proper principles be attended to in the selection of plants and the places into which they are introduced.'

He further remarks (p. 40),

'Among the plants which appear worthy of introduction from America into India, the Cinchonas are particularly desirable, and would no doubt succeed on the Nilgherries (read as Nilgiris), the different kinds of Ipecacuanha, as Cephaelis ipecacuanha, affording the best, and Psychotria emetica and herbacea, Richardonia braziliensis, rosea, and scabra, which give inferior kinds …'

3.1 In Calcutta and Neighbourhood

In 1849, Hugh Weddell, a Britain-born French botanist, observed that segments of either stem or petiole of *C. ipecancuanha* can strike adventitious roots when in contact with soil, thus indicating its vegetative-regeneration capacity. The first plant of *C. ipecacuanha* was received by Thomas Anderson, Superintendent of Calcutta Botanic Garden (CBG) (22°57' N, 88°37'E) from Joseph Hooker in Kew in 1868 and its propagation *via* vegetative means was with little success.

Thomas Anderson says (Anonymous, 1888 a, pp. 124-125):

8 December 1868: 'The plant of ipecacuanha originally introduced into the Botanical Gardens in 1866 is dead; but now I possess nine plants in this garden, which have been artificially propagated from the original one, besides five growing at the cinchona plantations in Darjeeling. To which place I sent one last year (*sic*. 1867). I have thus 14 plants of ipecacuanha.'

28 March 1870: 'The plants (*sic. C. ipecacuanha*) have thriven at Calcutta and at the lowest levels of the cinchona plantations in Sikkim and also at Ootacamund. There were 20 plants at Calcutta and Darjeeling last November, all the produce of one plant I received in 1866, and 13 at Ootacamund on the 9th of November last, the produce of three plants obtained by Mr McIvor[6] from Kew in 1866—67. These four original plants are the only ones from which cuttings have been made in India, all others having perished on the voyage, or soon after reaching the country'.

Some date later to 28 March 1870: 'I estimate that I shall be able to take out in January, 1871 (*sic*. to India, since Thomas Anderson was in UK on furlough at this time) not less than 50 plants of the true ipecacuanha, all of which will have been obtained in Europe, principally in exchange for rare plants and seeds from the Botanical Gardens, Calcutta'.

Unfortunately, Anderson could not carry out his plans. He died in U.K. while on furlough in 1870. George King succeeded Anderson, who officiated as the relieving Superintendent of CBG during Anderson's absence from Calcutta.

King (Anonymous, 1888a, p. 125) says:

1871: 'At the beginning of … 1871 the total stock of ipecacuanha amounted to five plants in Sikkim and seven in this garden (*sic*. CBG). From the five plants at Sikkim, 400 cuttings were obtained, the greater proportion of which have formed good roots, and are now healthy little plants. Five Wardian cases containing about 100 plants were received from Dr. Balfour (*sic*. John Hutton Balfour) and three cases from Messrs Lawson. … with orders from the Government of India, …, these plants have been forwarded to Sikkim as soon as practicable after their arrival here. The Calcutta climate having proved totally unsuitable to this plant, and the cultivation of ipecacuanha has been accepted like that of cinchona, as an experiment, which must form an outlying charge. … the propagation is being carried on chiefly in one of the hot, deep valleys on the outer slopes of the Sikkim Himalaya, which open towards the terai.'

Vegetative regeneration in *C. ipecacuanha*, casually observed earlier by Hugh Weddell, was confirmed by James McNab (Royal Botanic Garden, Edinburgh) in 1870 after laboratory trials (Balfour, 1872). The McNab trials enabled the production of several young plants of *C. ipecacuanha* leading to their dispatch to India in 1871. Two hundred and fifty-eight plants, thus generated in Edinburgh by McNab, were sent to India and were established in Rungbi Valley (Darjeeling District, *c.* 900 m amsl, 22°07' N, 88°26'E) in 1872 (Bentley and Trimen, 1875;

6 William George McIvor came Madras to organize, develop, and supervise the Ooty Botanic Garden (OBG) in 1845. He died in Ooty in 1876 and is interred in St Stephen's Church cemetery, Ooty.

Anonymous, 1888a).

The numbers of *C. ipecacuanha* established in India by 1874 was 63,423. King reports (Anonymous, 1888a):

> 28 April 1874: 'The cultivation has been practically confined to Sikkim, where it has been conducted chiefly by Mr Jaffrey[7] of the cinchona establishment, to whom is largely due the credit of its success. … Until the mode of propagating this plant by root and leaf cuttings was discovered, progress was extremely low. Since this discovery it has been proportionately rapid. … Mr Gammie, the resident manager of the cinchona plantation, and I quite agree that the ipecacuanha plant cannot be successfully cultivated in Sikkim except in shady places. In open spots where it gets full sun it soon becomes sickly. It is an essentially tropical plant and evidently prefers moist, shady spots where there is much vegetable mould in the soil, and an equitable steamy (*sic*. humid) atmosphere. A few plants had been sent to the Khasi Hills, and 100 are about to be dispatched to the Madras Government for trial in the garden at Barliyar, a low-lying, moist spot in one of the valleys of the Nilgiris.' 4 June 1875: 'The propagation of the plant by root-cuttings is now thoroughly understood, and there are in the hot-beds, under Mr Jaffrey's care, at Rungbee (*sic*. Rungbi) more than 100,000 young plants, while two years ago there were less than 7000.'

> 7 June 1876: '… I supplied a quantity of the drug (the dried root) to the Surgeon-General for trial in hospital practice. This was carefully administered in cases of dysentery by Dr Crombie, late officiating physician to the Medical College Hospital, and was pronounced by him to be quite as efficient as the best South American drug.'

> 10 July 1878: 'A number of plants have been sent to the Botanical Garden at Singapore, which enjoys a climate that ought to suit ipecacuanha perfectly. … We have been perfectly successful in propagating this plant from root-cuttings and seed, and it grows luxuriantly under cover. But out of doors the low night temperature of the cold weather proves too severe for it.'

> 10 July 1879: 'I have been obliged to give up all hope of the profitable cultivation of the drug in Northern India, the climate being unsuitable.'

The Kew Bulletin of Miscellaneous Information (Anonymous, 1888a) includes a summary of the report sent by James Gammie from Darjeeling[8] to the Director of Kew Garden on 11 November 1886. The same paper has the following to say (p. 127), which impresses as valuable in today's context of cultivation of alien plants in new environments:

> '… illustrates in a striking way the varied fortune which attends the attempts to introduce a plant to new physical conditions in a part of the world distant from its original home, and the impossibility of absolutely forecasting the event of the experiment even under the most discouraging circumstances.

Key points from the Gammie report as presented in the Kew Bulletin of Miscellaneous Information (Anonymous, 1888a) are summarized here: The original stock of *C. ipecacuanha* came from Kew and Edinburgh, most from Edinburgh. The plants from Kew differed strongly in their morphology from those that came from Edinburgh. Gammie cultivated them in a mixed manner in their trial farms (for every 10 of Edinburgh plants, one Kew plant) in the open, but shaded places, allowing them to take 'their chance'. Although initially the Edinburgh plants showed signs of vitality, soon, they 'disappeared' (so says Gammie), whereas the Kew plants, although fewer in number sustained. As of 1886, a good stock of plants (of Kew source?), 'in perfect health' (words of Gammie, again) existed, mostly under the shade of trees (*Cinchona*?) at 1400' (425 m), although their growth was slow. Economic viability could still be hopeless. Hardier varieties than the 'Kew' plants were to be found for establishment in new environments.

[7] Except that Mr Jaffrey was involved with the cultivation of *Cinchona* (*officinalis*?) in Darjeeling, no further details available.

[8] James Alexander Gammie (1839—1924) was a Kew gardener in 1861 became the Manager, Government Cinchona Plantations, Sikkim, in 1865 and was the Deputy Superintendent, Cinchona Department until 1897. From 1879 he collaborated with Charles H. Wood on the extraction of cinchona alkaloids.

George King's remarks, made in 1879, present a discouraging picture of *C. ipecacuanha* cultivation trialled in India; yet, the subsequent remarks of James Gammie present an encouraging picture. Nevertheless, a presentation made by Francis Ransom, a popular natural-product chemist of Britain, at an annual conference of British Chemical Society in 1887, indicates that the emetine level in the roots of *C. ipecacuanha* of Indian source was 1.7%, matching equally and impressionably with the emetine levels of *C. ipecacuanha* roots of Brazilian source (Anonymous, 1888b).

3.2 In the Nilgiris and Neighbourhood

William McIvor's efforts to grow *C. ipecacuanha* in the Nilgiris (11°25' N, 76°41'E) were considered more hopeful than those made by George King and associates in Calcutta and its neighbourhood. McIvor planted a few of *C. ipecacuanha* supplied from CBG (number not known) in the Burliar Experimental Garden, which was established by E. B. Thomas, Collector of Coimbatore—Nilgiris District in 1871, in Burliar (13°09'N, 80°29E', 800 m asl, the Nilgiris). Alexander Lawson[9], Superintendent of the Government Nilgiris Cinchona Plantations from 1882, remarks that *C. ipecacuanha* could not be grown in Burliar as an article of commerce. However, Lawson changed his view after planting a few of *C. ipecacuanha* in Nilambur (11°27' N, 76°22'E, presently in Mallapuram District, Kerala) in 1885-1886[10] (Watts, 1889, p. 248):

> '… growing very vigorously in the teak forest of Nilambur, the climate of which seemed to suit it much better than that of Burliyár'since the number of *C. ipecacuanha* in Nilambur trials increased from 200 to 700.'

Two years after the death of McIvor in Ooty, in 1878, George King of CBG visited the Burliar Experimental Garden and the Nilambur site where *C. ipecacuanha* was cultivated, although on a smaller scale than in CBG and its neighbourhood. King, based on this visit, says (Watts, 1889, p. 249):

> 'These were very healthy indeed, and I pressed on the overseer in charge of them the advisability of growing ipecacuanha there on a large scale. The matter has, I believe, lately taken up by Dr. George Bidie, Surgeon General of Madras. Some good results from the impetus given to the cultivation in Madras by that officer (*sic*. G. Bidie) may, therefore, I think, shortly be forthcoming'.

In a communication dated May 1887, George Bidie[11] writes (Watts, 1889, p. 249),

> 'It appears to me that the time has arrived for India to cultivate her own supplies of this precious root as in the case of cinchona, so as to be no longer dependent, may at any time interrupt the supply.'

4. Conclusion

Most of *C. ipecacuanha* farming in India occurs along the hill tracts of West Bengal (Garibas, Mongpoo, Darjeeling District) (Choudhury, 1951; Gupta, 1952) and to a small extent in parts of Assam and Sikkim (Goswami, 1963). The present-day cultivation of *C. ipecacuanha* in Mungpoo is mostly done within *Cinchona* plantations (Ananda Mukhopadhyay, Darjeeling, personal communication, email 21 March 2016), as was the practice a century ago.

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[9] Alexander Marmaduke Lawson (1840 – 1896), while teaching botany at the University of Oxford, was offered the post of Superintendent of the Government Cinchona Plantations, the Nilgiris, in 1882. He remained in the Nilgiris until shortly before his retirement and death (in Madras) in 1896. He is interred in St. George's Cathedral cemetery, Madras (Cotton 1945).

[10] Cultivation of economically important plants at Nilambur was initiated by Henry Valentine Conolly, the collector and magistrate of the District of Malappuram (formerly Malabar of the Madras Presidency, and today of Kerala State) in 1848. He established *Tectona grandis* (Lamiales: Lamiaceae) here and this site is popularly known as the Conolly's Plot. High-quality teak was harvested here.

[11] Surgeon General George Bidie (3 April 1830 – 19 February 1913) was a British physician attached to the Madras Medical Service. He superintended the Madras Government Museum (1872 – 1885) succeeding Jesse Mitchell (see Raman 2011).

The Government Emetine Factory, established in 1964, functions in Mungpoo. The Directorate of Cinchona & Other Medicinal Plants of West Bengal manages *C. ipecacuanha* cultivation (Government of West Bengal, 2012). Commercial production of *C. ipecacuanha* in India was 9–10 metric tons/year in 1982 declining by half of what Sundaresh (1982) referred as 1979 statistics. Most of Indian production was (is) used for domestic production of emetine and little is exported (Panda, 2002, p. 30). No *C. ipecacuanha* is grown in southern India, although initial trials were made in the Nilgiris and Nilambur.

After the pioneering work of Leonard Rogers in Calcutta, emetine was used extensively as injections of emetine hydrochloride, in spite of the then known side effects such as abdominal cramps, dizziness, vomiting, and pain at the site of injection. Keene *et al.* (1987) clarify that emetine inhibits protein and DNA syntheses. With the discovery of nitroimidazole compounds, emetine's value in treating amoebic dysentery has diminished today. Nevertheless, new uses for emetine in other spheres of health management, such as, in inducing apoptosis in leukaemia cells, are being found (Möller *et al.*, 2007).

Amoebic dysentery continues to haunt people in several tropical countries even today. We presently know that besides many recognized strains of *E. histolytica*, species such as *E. dispar, E. moshkovskii, E. coli, E. hartmanni*, and *Endolimax nana* occur in human intestine. *Entamoeba gingivalis* occurs in mouths and induces periodontal disease (Lucht *et al.* 1998). Usually *E. histolytica* infection is acquired by the consumption of either poorly cooked food or unclean water that will invariably include *E. histolytica* cysts[12], which induce amoebic colitis and liver abscess. The encysted trophozoites invade intestinal epithelium and induce the disease by damaging epithelial cells. Petri and Singh (1999) enumerate the differences between the biochemical pathways of *E. histolytica* and those of other similar eukaryotes, as the lack of glutathione, use of pyrophosphate instead of ATP during glycolysis, production of a unique alcohol-aldehyde reductase, and the inability to synthesize purine nucleotides *de novo*.

Early trials involving *Carapichea ipecacuanha* in treating amoebic dysentery, more of a 'nuisance, illness than a fatal illness today, and the efforts made by the British Government to introduce it into India along with *Cinchona* from South America (Raman, 2012) make a fascinating story, especially in reconstructing one milestone in the evolution of health management in India.

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[12] Cyst in Protozoa refers to 'oocyst', which is a hardy phase in protozoan lifecycles. A cyst is a resting spore, which on reaching the correct destination will release several infective cells, known as the trophozoites, capable of independent living.

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