INFECTIONS IN THE HISTORY OF MEDICINE

The history of Gin and Tonic; the infectious disease specialist long drink

When gin and tonic was not ordered but prescribed

Running title: The history of Gin and Tonic

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SUMMARY

Winston Churchill statement promoting *Gin and Tonic* as a life saver during British Empire extension hides many truths. As a matter of fact, the modern cocktail is thought to be born in India where it was widely distributed by Royal Navy for its anti-malarial properties. The aim of the present work is to review and unveil the history of Gin and Tonic through the centuries. As a matter of facts, primitive Gin and Tonic protective effects were well understood by physicians far before the advent of the "germ theory" and its fortunate invention is one of the most fascinating approaches in the history of preventive medicine. Indeed, *quinine*, a compound with protective effects on the replicative cycle of *Plasmodium spp* was discovered in 18th Century and since 19th it become the main compound of *tonic* beverages such as Schweppe's ones. Interestingly, it was administered to British expatriates seamen and soldiers in order to prevent febrile paroxysms. Soon after, British military doctors demonstrated that the addition of lime or lemon peels to *tonics* was effective in preventing scurvy. While, addition of alcoholic beverages and gin contributed to make more enjoyable the bitter and unpleasant taste of this beverages. Results: The spectacular voyage of Gin and Tonic teaches us that a popular recreational drink of our Century was a powerful prophylaxis which certainly helped British colonial expansion.

Keywords: malaria, prophylaxis, tropical medicine, quinine, military medicine

Introduction

Winston Churchill once declared: "*Gin and tonic has saved more Englishmen's lives, and minds, than all the doctors in the Empire*." The "*saving lives*" statement shocks us, as it shifts the perspective of this familiar long drink from recreational to a medical sphere. The reader might have heard some friends complaining about the taste of Gin and Tonic that resembles medicines with its bitterness. This should come with no surprise as Gin and Tonic saved uncountable lives since it was used as anti parasite prophylaxis for centuries [1]. The aim of this paper is to comment on Gin and

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Tonic history and remind us that this famous long drink, before being sold at seashores and in overcrowded clubs, has been a drug for decades.

Malaria occupies a unique place in the annals of history. Since *Homo sapiens* moved away from hunting and gathering to sedentary communities, humanity has paid a remarkable death toll to arthropod born diseases, including those transmitted by mosquitoes [2]. As a matter of fact, we have started to cultivate fields and engineer the environment; thus creating the perfect habitats for mosquito propagation [3]. Moreover, where Europeans established crowded settlements and backwater, malaria flourished, resulting in season illness and weaker communities [4, 5]. Interestingly, one of the major roles played by malaria in human history lies in its proven role in shaping and altering the course of wars and empires. Indeed, a body of literature depicts malaria as a weapon, sometimes playing in favour and other times against the expected outcomes of different historical events [6, 7, 8]. Interestingly, this was well understood by physicians also before the advent of the "germ theory" leading to some curious, fascinating and probably fortunate approaches of preventive medicine like the one we are going to disclosure.

The serendipitous' medical discovery of quinine

As a matter of fact, the quinine discovery and its usage to heal people with malaria is still controversial, mainly in its early stages. Certainly it happened on the other side of the Atlantic Ocean, during the occupancy of the so-called New World. Quinine is the first anti-malarial drug of modern medicine and remains an important drug almost 400 years after its effectiveness was first documented. This story starts in the "new indies", during the occupancy of the so-called New World. Here, quinine was discovered and used to heal malaric people at early stages. As Achan and colleagues brilliantly stated, its discovery is considered the most serendipitous medical discovery of the 17th century [9]

"*In the district of the city of Loja, diocese of Quito, grows a certain kind of large tree, which has a bark like cinnamon, a little more coarse and very bitter, which, ground to powder is given to those*

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who have a fever, and with only this remedy, it leaves them." Bernabe Cobo (1582-1657), a Spanish Jesuit missionary and writer (Historia del Nuevo Mundo; cited by Greenwod et al) [10].

According to the first legend, a native American with a high fever was lost in an Andean forest. Thirsty, he drank from a pool of stagnant water finding a rare bitter taste. Soon he realized that the water had been contaminated by the surrounding Cinchona tree – *Cinchona officinalis* (quina-quina in Amerindian) [1]. Surprisingly, his fever soon abated, and after sharing his story with fellow villagers, the community started to use quina-quina bark extracts for the treatment of fevers [9, 11, 12]. Chinchona trees are medium sized plants with glossy evergreen leaves and fragrant white, pink, purple or red flowers; their bark were classified by botanists according to their colour and alkaloids content [1]. Their bark is rich in quinine and evolved to protect plants from insect consumption [1]. The use of cinchona bark for treating malaria only started following the Spanish subjugation of Peruvian communities, as there is no evidence that malaria existed in the New World before Europeans arrival [13]. There are many arguments supporting the idea that malaria worst form, caused by *P. falciparum,* was a 17th Century import from Europe and slavery trade [13, 14, 15]. Furthermore, Chinchona trees grow at high-altitudes in the Andes apart from malaria-ridden lowlands where natives were most affected [1]. Another story reports of the Countess of Chinchon (1576-1639), wife of the Viceroy of Peru, that was cured from the "*ague" (*meaning a fever such as malaria and marked by paroxysms of chills) using a native remedy extracted from the bark of quina-quina tree (Figure 1). Even if this account does not mirror the real facts happened, the Countess was immortalized by Linnaeus, the Swedish taxonomist, when he gave the tree its botanical name, *Chinchona* genus in *Genera Plantarum* [16]. Several legendary stories about quinine and Chinchona tree remedies got lost in the mist of the time making difficult to assess the value of cinchona bark real discovery. One possibility lies the fact that cinchona bark were drunk by the Peruvian natives to suppress shivering when exposed to dampness and cold [17]. The concept of use a "hot" infusion to treat a 'hot' - febrile - disease like malaria was against 17th century medical doctrine, but it would be quite in order to try the infusion, by analogy, in the shivering stage of

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malaria rigors, demonstrating efficacy [10]. Far before being characterised as a compound from the bark of the cinchona tree, quinine was used to treat malaria from the early 1600s. At the time such remedy was called "Jesuits' bark," "cardinal's bark," or "sacred bark." These names derived from its use in 1630 by Jesuit missionaries in South America [9].

"[...] made into powder (the bark) and given as a beverage, cures the fevers and tertians; it has produced miracolous results in Lima" these are the words of Father Antonio de la Calancha (1584–1654), a priest based in Peru [18].

Figure 1 - The Count of Chinchon receiving Chinchona-root from a Peruvian Indian. Fresco painting in the Ospedale di Santo Spirito, Rome. Wellcome Images

The long pathway of malaria: the role of the quinine

Although the mosquito-parasite cause of malaria was not understood until the end of the nineteenth century, fevers were known and classified in past centuries according to their pattern [19]. Remarkable is the work of the Italian physician Francesco Torti (1658-1741) who published a precious family tree of fevers, the *Lignum Februm* [20], a stylised cinchona tree where "*agues*" were classified based on their response to chinchona barks. Isolation of the major natural alkaloids of cinchona bark, notably quinine and its stereoisomer quinidine, was achieved by Pierre Pelletier (1788–1842), Professor of Toxicology, and Joseph Caventou (1795–1877), Professor of Chemistry

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at the Ecole de Pharmàcie in Paris. This happened in in 1820, one hundred years after the first observations and reports regarding Chinchona bark effects on fever [10]. The discovery paved the path for quinine mass utilisation for fever cure, the bark of the cinchona tree was first dried, ground to a fine powder, and then mixed into a liquid (commonly wine or port) before being drunk. Herbs such as cinnamon, cloves and oranges were used to mask its bitter unpleasant taste, which was hardly accepted by sick people [1, 9].

Quinine is a short-acting medication where a single oral dose maintains a measurable drug concentration for a matter of hours not days [21, 22]. In therapeutic doses, it often causes a set of unpleasant symptoms known as cinchonism which includes tinnitus, vertigo, headache, dysphoria, nausea, and vomiting [22]. Quinine and other cinchona alkaloids including quinidine, cinchonine and cinchonidine are all effective against *Plasmodium spp*, the causative agent of malaria [9]. The efficacy of these four alkaloids was proven in one of the earliest clinical trials, conducted from 1866 to 1868, in 3600 patients using prepared sulphates of the alkaloids. With the principal outcome measure of "cessation of febrile paroxysms", all four alkaloids were found to be comparable, with cure rates of >98%. However, after 1890 quinine became the predominantly used alkaloid, mainly due to a change in supply from South American to Javan cinchona bark, which contained a higher proportion of quinine [23. 24].

Malaria, war conflicts and military medicine

British East India Company (EIC), started as a trading company, used its military might and aristocratic influence to conquer Indian empire at the very moment its Atlantic empire was plunged into crisis by the American Revolution (1765-1783). Unfortunately for the EIC, more British soldiers displaced in the new subcontinent died of malaria than battling the local armies trying to contain their expansion [25, 26]. During the 18th Century, malaria gradually became accepted as a defined set of intermittent fevers responding to ‘therapeutic tests*’* using *C*inchona bark or, from the 1820s, by using quinine. As a consequence, during the decades of EIC occupancy and expansion

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quinine powder became critical to the health of the British Empire [27]. By the 1840s, British civilians and soldiers in India were using 700 tons of cinchona bark annually for quinine extracting [28]. The paths of malaria and quinine in nineteenth-century British India were so untangled that Rohan Deb Roy brilliantly defined them as "locked in symbiotic bonds of co-determination" [29]. Up to the mid-end of nineteenth century, quinine antifebrile properties were well recognised and quinine was used to cure "*agues*" diffusion in Europe and in the overseas colonies. Thus, malaria endemicity and its constant death toll, mainly overseas, might have posed the attention to the so-called Preventive Chemotherapy; its task was to avoid and not only cure tropical agues. Indeed, The British Navy from the eighteenth century occasionally used quinine in a preventive perspective but it was not a formal prophylaxis until 1854, when the army physician Captain William Balfour Baikie (1824-1864) ordered every European man under his responsibility to take a daily dose of quinine during the exploration along Niger river. Incredibly, no deaths were registered [30, 31]. From here, quinine prophylaxis become the kind of technology able to overcome the obstacles of nature encountered by Europeans when venturing into new places and climates (Figure 2). Malaria prophylaxis together with weapons and military tactics depicted the art of war of nineteenth century [1, 32].

Contemporary to the diffusion of quinine medicaments distribution, private companies started to produce and trade tonics for medical purpose. *Tonics* were fashion carbonated beverages containing different kind of chemicals to which different properties were attributed. Tonic must not be taken too literally since none of the ingredients of the traditional tonics has the pharmacological effect of increasing tone. As a matter of fact, a tonic is best defined as a preparation given to promote a feeling of well-being [33]. In this growing market of sparkling drinks, the well-known "Tonic water" was born; a sugar bubble water, flavoured with fruit essences and a small addendum of quinine [34]. Erasmus Bond introduced the first commercial tonic water in 1858 and it was soon followed by introduction in 1870 of "Indian Quinine Tonic" by Schweppes company. Johann Jacob Schweppe (1740-1821), a German-born chemist settled in Bristol, was the main producer of tonic

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water [28, 35] selling a product containing 30 mg of quinine per pint [36]. Obviously, the British East India Company and the British Army soon adopted the tonic and mixed the product with lime, which had the added value of preventing scurvy, another plague in the colonies and during intercontinental ships [34, 37]. As a matter of fact, the scot surgeon James Lind (1716-1794) was the first to really prove the efficacy of citrus juice as a treatment for scurvy in 1747 [38]. We now know that the quinine concentration in the blood after 2h hours following the consumption of 500-1000ml of tonic water is approximately 0.2 mg/l. Its therapeutic range is unusually broad, from 0.2 mg/l to 2.0 mg/l, because of the varying drug susceptibility of different *P. falciparum* strains; thus, demonstrating suboptimal parasitocidal effects of tonic water. Considerable quantities of tonic water may, for a short period of time, cause transitory suppression of parasites [34]. However, continuous levels that are appropriate for malaria prophylaxis cannot be maintained with even large amounts of tonic and to obtain the required amount of quinine one would need to consume approximately 70 litres of tonic water [34, 39]. It is worth noting that tonic water today has considerably lower levels of quinine than used in earlier preparations.

Figure 2 - The benefits of using quinine, illustrated by the homecoming of a soldier. Wellcome Collection gallery.

Gin (Jenever): a companion to the war

As depicted in the previous chapters, Tonic water and quinine additioned beverages became widely distributed in the English colonies because of their anti-malarial properties and relative ease of production. However, how was it possible to convince masses of soldiers and sailors to undergo

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such an acidic, bitter and unpleasant prophylaxis? Since now we have depicted how and why tonic water was introduced in British army for its properties; thus, the question rising at this point of the lecture is how Gin was coupled with this new born prophylaxis. G*in* or more precisely *Jenever* (juniper in Dutch) is considered to be developed at the University of Leiden in Netherlands by Franciscus de la Boe (1614–1672), a pioneer in circulatory medicine, who was trying to demonstrate beneficial effects of different botanical extracts [40]. Traditionally alcohol had been used by the troops to cope with the traumatic stress of battle but also as a way of softening the transition from the experience of combat to safe routine. Indeed, the use of alcohol had divided medical opinion with some doctors viewing it as harmful to occupational function, and to health; while others argued that alcohol contributed to lifting morale, aiding unit cohesion and protecting soldiers from mental disorders [41]. It is known that during the Thirty Years War (1618-1648) *gin* was provided to continental soldiers for its calming effects when going into battle; reason why the alcoholic was also termed 'Dutch courage'. By the time English soldiers arrived in Holland in 1618, *jenever* was widely drunk between Dutches, especially in the form of a malted grain-based spirit flavoured with juniper berries. Furthermore, it was marketed at the time as a treatment for a variety of health problems including stomach pains, gout and as a morale boosting [42]. Shortly after, the new-born product was renamed "gin" in the British islands [1, 40]. There is evidence that during 18th Century alcohol consumption was controlled and discouraged in British Military apparatus, as showed by Smith and colleagues thanks to an archaeological approach [43]. Nevertheless, between 1695 and 1735 hundreds of small gin-distilleries flourished in Great Britain resulting in a drinking frenzy, known as the "Gin Craze", that mostly affected the poor communities having easy access to cheap gin variants [42]. In 1733 London alone produced eleven million gallons of legal gin, enough for fourteen gallons per person per annum (equal to 4,4 litres per person per month). The period was so unsettling, that some scholars have linked this Gin Craze to the crack epidemic in 1980s America [40].

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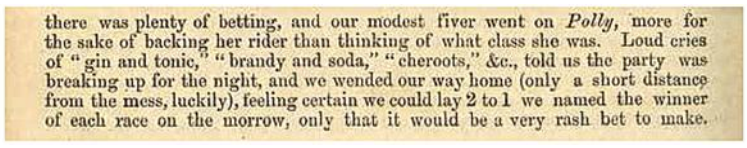
It is in this moment of history that the British Navy started encouraging alcohol consumption for soldiers, bringing to light the Gin and Tonic as we know today. Indeed, "Empire" intrinsically include soldiers and civilian expatriates eager to recreate the civility of home (Figure 3). In the 18th Century, Royal Navy was alcohol-based classed; with seamen drinking rum or beer and officials drinking gin [39]. In general, products containing quinine have a bitter, almost unpleasant taste and historically were mixed with wine or other alcoholic beverages (e.g. Malaga Quina - Spain; Cap Corse - France; Barolo Chinato - Italy). To get around this problem, British officers in the Indian Army added sugar and a shot of gin to quinine, creating the basis of Gin and Tonic [35, 37]. Also earlier "mixing" experiments are known. Indeed, during the American Civil War certain army surgeons recommended the administration of half a gill of whisky, containing quinine in a concentration of 2-4 grains, served twice daily to every man in the command [44]. Moreover, William Buchan, a famous Scottish physician (1729–1805), wrote: "*Take an ounce of the best Jesuits' bark, Virginian snake root, and orange peel, of each half an ounce; bruise them all together, and infuse for five or six days in a bottle of brandy, Holland gin, or any good spirit; afterwards pour off the clear liquor, and take a wine-glass of it twice or thrice a day.*" [10]. The Royal Navy continued to use gin as a creative way to subminister quinine, and culture grew up around it. As a matter of fact, when ships docked, they used to show a green and white flag to signal an open invitation to "*come aboard and share a drink*" for officers in the port [40]. Interestingly, the first known reference to gin and tonic as a bar cocktail is in the Anglo-Indian *Oriental Sporting Magazine* in 1868. The term was evidently a familiar phrase in India, being called out by attendees of a horse race at Sealkote (Sialkot), present day Pakistan, as they finish for the evening [1].



there was plenty of betting, and our modest fiver went on *Polly*, more for the sake of backing her rider than thinking of what class she was. Loud cries of "gin and tonic," "brandy and soda," "cheroots," &c., told us the party was breaking up for the night, and we wended our way home (only a short distance from the mess, luckily), feeling certain we could lay 2 to 1 we named the winner of each race on the morrow, only that it would be a very rash bet to make.

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Figure 3. The first known reference to 'gin and tonic' in print. *Oriental Sporting Magazine* (1868). University of Minnesota Libraries.

Gin and Tonic: a metaphor for empire

This spectacular voyage of Gin and Tonic started in Perù and crossed continents reaching Europe and the Indian subcontinent. Sailboats were the vehicles of this narration and displaced armies the main recipients. It was born as a jumble of expedients to promote health, thus rapidly becoming a potent prophylaxis which certainly helped British colonial expansion. Quinine and the fight against malaria in India have been defined as a biopower deeply connected with military and economic aspects of British India rule [29]. Thus the success of the colonial expansion could have been shaped by what Nicole Shukin calls a '*zoopolitics*' involving insects, firstly mosquitoes. As proposed by Nicole Shukin quinine, as well as Gin and Tonic in our opinion, looks like a metaphor for empire: bitter, expensive and transformative, which could be mutated variously to appear as charitable, reasonable and even palatable [45]. Primary distributed in military fields during past centuries and sold only for recreational use nowadays (Figure 4, Figure 5).

Conclusions

The trip we unveiled to the reader is certainly twisting and rich of diversities. Nevertheless, a continuous underlying medical condition accompanied this travel, seeking for modern remedies. This sort of Ariadne's thread is malaria and its death toll. Interestingly Karen Masterson proposed that Mosquitoes control our behaviour because we have yet to control them [5]. As we described above, the history of quinine and Gin Tonic development shows as a protozoan infective disease could shape the costumes and behaviours of people also after centuries. To our knowledge it is the first time that a drink is introduced in everyday life after an initial anti-parasitic usage in medicine; although, infective disease are known to have shaped human food costumes [46]. Interestingly Gin Tonic may retain this ambivalence: long drink and drug. As a matter of fact, it could definitively be defined an old fashioned drug. As Jacques Derrida once noted, in order for particular substances to

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be classified as drugs, a history is required together with culture, conventions, evaluations and entire network of intertwined discourses, norms and rhetoric [47]. Close your eyes for a moment, rewind the film of past centuries and think about the fascinating imprinting that malaria and quinine left in our societies when choosing the next drink.

Figure 4. The origins of quinine product distribution for prophylactic usage. Taken from Wikimedia Commons

Fig 5. Nowadays recreational consumption of quinine-based cocktails. Taken from Wikimedia Commons

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Data availability:

Figure 1. Taken from Wikimedia Commons, the free media repository. Available at https://wellcomeimages.org/indexplus/obf_images/8a/26/7356dc443c4e88bd8241bf75b05b.jpg.

Figure 2. Taken from Wikimedia Commons, the free media repository. Available at https://wellcomeimages.org/indexplus/obf_images/45/75/3e27fecba45b0fc30db451ede7ec.jpg.

Figure 3. Public domain image from University of Minnesota Libraries. **Fig 4.** Taken from Wikimedia Commons, the free media repository. Available at https://commons.wikimedia.org/wiki/File:%C3%89cole_des_r%C3%A9ugi%C3%A9s_d%27Asie_mineure_et_de_Mac%C3%A9doine_distribution_de_quinine_ao%C3%BBt_1916.jpg. **Fig 5.** Taken from Wikimedia Commons, the free media repository. Available at https://commons.wikimedia.org/wiki/File:Patr%C3%B3n_cocktail_bar_(5807919992).jpg

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