

Finding Cures for the Emerging Yaws: Analysis of Kitab Tib Muzium Terengganu and MSS1292

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Abstract

Yaws is a neglected tropical disease infecting underprivileged population living in tropical and subtropical regions. The disease has persisted in low-developed countries and now emerges in Europe due to increase in travel and economic factors. The threat of yaws is demonstrated by the emergence of antimicrobial resistance strain necessitating the pursuit of new cures. In this study, we used Malay medical manuscripts Kitab Tib Muzium Terengganu and MSS1292 to identify possible treatment for yaws. Malay terms synonymous with *puru*, are listed and categorised in terms of routes of administration and methods of preparation for the remedies. Comparative analysis using modern scientific database Pubmed was performed to find support for the use of the Malay *materia medica*. The study identified 17 formulations from the manuscripts for three types of yaws. The most common materials mentioned in the Malay medical manuscripts are *terusi* (copper sulphate), *tempurung* (coconut shell) and *kunyit* (*Curcuma longa*); *belerang/belerang bang* (arsenic sulphide), *beras* (rice), *lada/lada sulah* (pepper) and *tuba tikus* (arsenous acid). Comparative analysis found that there were no reports on the use of these materials as yaws treatment which open a huge potential for medical research using manuscript data for the treatment of yaws.

Key words: *Puru*, Malay manuscript, neglected disease, skin disease, *Treponema pertenu*, wound healing.

Introduction

Yaws is a chronic bacterial infection caused by infection with *Treponema pallidum* subsp. *pertenue*. It forms part of a group of infections caused by treponemal species that include endemic syphilis, bejel and pinta (Mitjà & Mabey, 2019). The disease is found primarily in deprived communities in tropical and forested areas of Africa, Asia, Latin America and the Pacific. Poor socioeconomic conditions facilitate its spread. Yaws clinically presents as lesions of the skin, bone and cartilage. Without treatment, it can lead to gross deformities and disabilities.

There are basically two stages of yaws disease. The primary stage of yaws appears after a variable incubation period (mean of 21 days after exposure) as a solitary erythematous papule that can grow into a papilloma (benign lump) of 2 to 5 cm in diameter by peripheral extension (Mitjà, Asiedu, & Mabey, 2013; Mitjà et al., 2015). The primary lesion, called "mother yaw" is not painful but may be pruritic. The mother yaw is highly contagious and can persist for weeks or months before healing spontaneously. Regional swellings of lymph nodes and arthralgia (joint pain) may also occur. Secondary manifestations of yaws appear due to the pathogen's systemic dissemination during early infection, which can occur months after the primary lesion, or can also be delayed as long as 1 to 2 years from the initial exposure. Secondary papules, although smaller, may resemble the mother yaws or may appear as scaly maculae of irregular shape. The daughter lesions can also expand and ulcerate, releasing a highly infectious fluid (Mitjà et al., 2015).

In 1948, health experts were optimistic that yaws can be eradicated. The World Health Organization (WHO) set 2020 for global eradication of yaws (Mitjà et al., 2015). However, to date, the disease remains persists in many parts of the world due to negligence on its treatment and eradication. WHO reported that up to 2013, 13 countries were known to be endemic with yaws; with 3 additional countries reported confirmed cases (Boock, Awah, Mou, & Nichter, 2017; Dofitas, Kalim, Toledo, & Richardus, 2020) and 3 countries reported suspected cases of yaws (World Health Organization, 2021). Yaws has also emerged in Western countries mainly due to Westerners visiting yaws-endemic countries and residents from yaws-endemic countries travelling as migrant workers (Calleri, Angheben, & Albonico, 2019).

Yaws was also once prevalent across the Malay Archipelago. The Malay people use the term *puru* to denote gaping, difficult-to-treat wound associated with various types of *Treponema* infection. In several Malay dictionaries, *puru* is also interchangeably used with *sakit patik* or *sakit patek*, sometimes defined as *Framboesia tropica*, an infectious non-venereal disease of tropical climates with boils (*bisul*), dried wound (Malay: *luka yang sudah kering*) and scabies-like (*kudis*) skin diseases (Kamus Dewan Bahasa dan Pustaka, DBP; <https://prpm.dbp.gov.my/>) and Kamus Besar Bahasa Indonesia, KBBI; <https://kbbi.web.id/>). When used as a compound word, the term *puru* becomes specific, whether relating to a specific medical condition or to a specific stage of a disease. *Puru peringgi* for example, refers to syphilis (Mohd. Shafri, 2019), an infectious venereal disease caused by *Treponema pallidum* subsp. *pallidum*, which is different from yaws. Specific terms for yaws denoting the different stages or presentation of the disease could be found in medical dictionaries such as A Dictionary of Malay Medicine (Gimlette, 1939).

Emergence of strains of antimicrobial resistant to treat yaws (Beale et al., 2020) underlined the need for continuous search for yaws treatment. This study aims to analyse *puru* as defined in the *Kitab Tib* or Malay medical manuscripts and to compare the materials used for *puru* treatment with the modern medicine for treating yaws.

Methods

Malay terms for yaws were first identified from A Dictionary of Malayan Medicine (Gimlette, 1939). These were also compared with data from authoritative online and non-online dictionaries such as Pusat Rujukan Persuratan Melayu (www.prpm.dbp.gov.my) Kamus Dewan Bahasa dan Pustaka, Kamus Besar Bahasa Indonesia, and other publications.

Manuscript data were then categorised according to terms, treatment and formulations. Information on yaws and the list of plants and materials retrieved during this process was then searched in NCBI PubMed. Scientific or English names associated with the ingredients for the traditional remedies were based on findings from several sources (online dictionary of Pusat Rujukan Persuratan Melayu and The Plant List website (www.theplantlist.org)). Comparative analysis was then performed to compare the use of individual herb or plant mentioned in the Malay manuscripts to published papers in modern scientific database. This was performed using a combination of terms: [*puru*] OR [yaws] OR [*Treponema pertenue*] AND [scientific names or common names of each plant]. Further search was carried out using [scientific names and common names of each plant] AND [wound healing] OR [anti-inflammatory]. The inclusion criteria were any *in vitro*, *in vivo*, or randomised controlled trials on the anti-yaws, anti-inflammatory and wound healing activities of the selected plants.

Results

Yaws-related terms in Malay medicine

Technical terms of various types of *puru* were retrieved from A Dictionary of Malayan Medicine (Gimlette, 1939). In ancient Malay manuscripts, *puru* is a general term for various types of skin diseases, including ulcers, sores or yaws. The list from Gimlette is further short-listed to those that are specific for yaws. When compared to other authoritative dictionaries, the superiority of Gimlette's dictionary is clear. This is because Gimlette's dictionary is a medical dictionary written by a British doctor with long service in several states in the Malayan Peninsula. He had a deeper understanding and strongest motivation to study Malay medicine compared to other colonial researchers, exemplified in the dictionary through detailed descriptions of diseases, the accompanying terminologies and the ingredients to make medicine. Gimlette had other works of note such as Malay Magic and Charm which is also a treasure-trove for today's scholars of Malay medicine. The various description of *puru* related to yaws as noted by Gimlette is presented in Table 1.

Table 1: *Puru* related to yaws from A Dictionary of Malayan Medicine (Gimlette, 1939).

Terms	Explanation
1. <i>Puru dalam tulang</i>	Ulceration of bone due to tertiary yaws
2. <i>Ketut puru; puru ketut</i>	The initial, military, popular eruptions of secondary yaws, which comes out in successive crops and is attended by great itching.
3. <i>Puru ibu; ibu puru</i>	The largest, best developed, and most persistent sore of secondary yaws, but not necessarily the primary sore. Malay starts treatment when <i>puru ibu</i> diagnosed. Most commonly found below the waist, foot, leg, or thigh, but may occur on the wrist and hand. It leaves a scar which subsequently becomes dark in colour.
4. <i>Bunga puru</i>	The initial eruption of <i>ketut puru</i> (secondary yaws) into large sores covered with yellow, sticky crusts.
5. <i>Puru dedak</i>	One of the presentations of <i>bunga puru</i> of the secondary yaws. Presents as exaggerated scurfy condition of the initial popular eruption and very itchy.
6. <i>Puru kechar</i>	One of the presentations of <i>bunga puru</i> of the secondary yaws. Presents with eruption of rupial-shaped sores i.e. small sores capped with crusts. Benign and common. Not painful and resolve with treatment using <i>getah aguh</i> and <i>getah gam</i> .
7. <i>Puru siput</i>	One of the presentations of <i>bunga puru</i> of the secondary yaws. Synonymous to <i>puru kechar</i> .
8. <i>Puru kenam</i>	One of the presentations of <i>bunga puru</i> of the secondary yaws. Present as eruptions of circular red lumpy spots all over the body.
9. <i>Puru Burma</i>	One of the presentations of <i>bunga puru</i> of the secondary yaws. Synonymous to <i>puru kenam</i> .
10. <i>Puru kerbau; puru mata kerbau</i>	One of the presentations of <i>bunga puru</i> of the secondary yaws. Presents with very large flat sores.

11. <i>Puru kertas</i>	One of the presentations of <i>bunga puru</i> of the secondary yaws. Presents with serpiginous eruption which is distinguished from other forms by the general superficial nature of eruption. It is difficult to treat and can cause death in kids.
12. <i>Puru pitis</i>	One of the presentations of <i>bunga puru</i> of the secondary yaws. Presents with eruption of flat circular sores which are supposed to resemble the shape of a <i>pitis</i> coin.
13. <i>Puru sekam</i>	One of the presentations of <i>bunga puru</i> of the secondary yaws. Synonymous to <i>puru dedak</i> .
14. <i>Puru siput</i>	One of the presentations of <i>bunga puru</i> of the secondary yaws. Synonymous to <i>puru kechar</i> .
15. <i>Puru tak jadi</i>	One of the presentations of <i>bunga puru</i> of the secondary yaws. Suppressed yaws.
16. <i>Puru tapak anjing</i>	One of the presentations of <i>bunga puru</i> of the secondary yaws. Presents with sores arranged in the form of dog's footprints. Serious and painful variety of yaws in children.
17. <i>Sengal puru</i>	Pains in the fingers, joints and long bones.
18. <i>Bubul; puru lapeh</i>	Foot-yaws.
19. <i>Puru parang</i>	Deep ulceration in the foot of elderly people, or "chopper" yaws.

Formulation for yaws

A total of 17 medical formulations on *ibu puru*, *puru parang* and *puru dalam tulang* were retrieved from two Malay medical manuscripts: Kitab Tib MSS 1292 PNM (Mat Piah & Mustapha, 2019) and Kitab Tib Muzium Terengganu (KTMT; Hussain, 2019). *Puru parang* is mentioned in KTMT (n=9) and MSS 1292 (n=4) (Table 2). *Ibu puru* could be found in KTMT (n=2). *Puru dalam tulang* could be found in KTMT (n=2). Other terms of *puru* as listed in Table 1 could not be found in the Malay medical manuscripts.

Table 2: The distribution of formulations for yaws-related *puru* in KTMT* and MSS 1292 based on the modes of administration.

Mode of remedy administration	List of formulations		
	<i>Puru parang</i>	<i>Ibu puru</i>	<i>Puru dalam tulang</i>
Decoction or molded into small eaten medicine	KTMT 036.195.012	-	KTMT 036.197.022
	KTMT 036.195.017		KTMT 036.197.024
	MSS 1292.1		
Topical application	KTMT 036.194.001	KTMT 036.195.013	-
	KTMT 036.195.016	KTMT 036.195.014	
Body steaming	KTMT 036.194.009	-	-
	KTMT 036.195.011		
	MSS 1292.2		
	MSS 1292.3		
Inhalation	KTMT 036.196.018	-	-
	KTMT 036.197.025		
	MSS 1292.4		
Bath	KTMT 036.195.010	-	-

*Formulation numbers for KTMT are based on the numbering in the book. KTMT, Kitab Tib Muzium Terengganu

Various methods have been described to prepare the traditional remedies; scrubbing, grinding and pounding were the most popular preparation methods. In terms of modes of administration of the remedies, various techniques were used by the Ancient Malay people including oral remedy (n=5), topical (n=4), body steaming (*tangas*; n=5), inhalation (n=2) and bathing solution (n=1) (Table 2).

The most frequently mentioned materials used in the treatment of yaws are *terusi* (copper sulphate), *tempurung* (coconut shell) and *kunyit* (*Curcuma longa*) where each could be found in 3 different formulations, followed by *belerang/belerang bang* (arsenic sulphide), *beras* (rice), *lada/lada sulah* (pepper) and *tuba tikus* (arsenous acid), where each is mentioned in 2 different formulations (Table 3). Other *materia medica* are mentioned only once in either one of the Malay medical manuscripts. The number of materials used to treat yaws is between one to seven materials per each formulation. Each prescription uses different combinations of herbal, animal or minerals, except for KTMT 036.194.009 and MSS1292.2 which use two out of three similar *materia medica*. Both formulations are prescribed for body steaming to treat lesions of *puru parang* on the soles.

Table 3: Excerpts of formulations for *ibu puru*, *puru parang* and *puru dalam tulang* from the Malay medical manuscripts. Formulation numbers for KTMT are based on the numbering in Dermatologi Kitab Tib Muzium Terengganu (Hussain, 2019) and for MSS 1292 are based on the order mentioned in this study.

No.	Formulation No.*	Malay excerpt and English translation [source]	Materials (vernacular Malay/scientific names)		Remarks (A: Administration, DG: Dose regimen)
<i>Ibu puru</i>					
1	KTMT 036.195.013	<i>Jikalau hendak jadi ibu puru, maka ambil buah terung kemu dan hempedu sawa. Maka asah, bubuh kepada puru itu, aflat.</i>	<i>Terung kemu</i> <i>Hempedu sawa</i>	<i>Cyclea laxiflora</i> <i>Ouratea crocea</i>	A: Topical
		If it is going to be mother yaws, take <i>terung kemu</i> fruit and <i>hempedu sawa</i> . Scrub everything and apply on the lesion, (it will) heal.			
2	KTMT 036.195.14	<i>Sebagai lagi ubat ibu puru, ambil akar birah, akar cengkilan dan buah sirih dan cendana janggi. Maka asah bubuh kepada puru itu, aflat.</i>	<i>Birah</i> <i>Cengkilan</i> <i>Sirih</i> <i>Cendana janggi</i>	<i>Alocasia langiloba</i> Miq. <i>Croton tiglium</i> L. <i>Piper betle</i> L. <i>Pterocarpus santalinus</i> L.f.	A: Topical
		Another remedy for mother yaws, take <i>birah</i> root, <i>cengkilan</i> root, <i>sirih</i> fruit and <i>cendana janggi</i> . Then, scrub everything and apply on the lesion, (it will) heal.			
<i>Puru parang</i>					
3	KTMT 036.194.001	<i>Bab pada menyatakan ubat puru parang terlalu ajaib sekali anugerah akan Allah Subhanahu Wata'ala. Pertama ambil air, suruh basuh puru itu kepada orang itu. Mandi dahulu beri suci-suci. Sudah itu maka ambil daun ganja yang hidup segenggam erat. Maka giling, campur beras lumat-lumat. Maka buat bedakkan padanya tiga hari, jangan mandi, aflat.</i>	<i>Ganja</i> <i>Beras</i>	<i>Cannabis sativa</i> L. <i>Oryza sativa</i> L.	A: Topical DG: Apply on lesion for 3 consecutive days
		Another remedy for <i>parang</i> yaws, of superb effectiveness, a grace from Allah (God). Firstly, take water and use it to wash yaws. Ask the patient to take bath first. Then, take a handful of fresh <i>ganja</i> leaves and grind it finely.			

		Mix with finely pounded rice. Apply as powder for three consecutive days. Do not take bath within those three days, (it will) heal.			
4	KTMT 036.194.009	<i>Sebagai lagi ubat puru parang tumbuh di tapak kaki. Ambil daun rembega, tutuk lumat-lumat. Rebus dengan air, maka bubuh kunyit, tumbuk dahulu. Ketang teguh-teguh dengan daun pisang kelat. Apabila mendidih rupanya, maka pesapkan sedikit keluar asapnya itu. Kenakan tapak kaki yang puru itu asapnya itu. Maka buatlah barang dua kali atau tiga kali, demikian itu, aflat.</i>	Rembega Kunyit Pisang kelat	<i>Calotropis gigantea</i> (L.) Dryand <i>Curcuma longa</i> L. <i>Musa acuminata</i>	A: Body Steaming
		Another remedy for <i>puru parang</i> which appears on soles. Take <i>daun rembega</i> and pound it well. Boil it with water and add pounded turmeric. Tie it well with <i>daun pisang kelat</i> . When it has boiled, channel the steam from the boiled remedy towards the soles. Do it for two to three times, God will heal it.			
5	KTMT 036.195.010	<i>Sebagai lagi ubat puru parang yang gatal, maka ambil daun bintangor paya yang merah pucuknya. Maka rebus, embunkan, maka mandikan.</i>	Bintangor paya	<i>Calophyllum inophyllum</i> L.	A: Body bathing
		Another remedy for itchy <i>parang</i> yaws, take <i>bintangor paya</i> leaves of reddish shoot. Boil it and then let it in the dew. After that, bathe with it.			
6	KTMT 036.195.011 ¹	<i>Sebagai lagi ubat puru tumbuh di kaki. Maka ambil buah kecubung hitam atau putih yang masak. Bakar, sudah, maka diserkup dengan tempurung jantan. Maka wapkan pada kakinya yang puru itu kira-kira tanggung hangatnya. Perbuat barang empat kali berturut-turut pagi petang, aflat.</i>	Kecubung Tempurung (jantan)	<i>Datura metel</i> Coconut shell (male)	A: Steaming the affected body parts (feet) DG: Apply steam of the medicine for 2-4 days consecutively, both in the morning and in the afternoon.
		Another medicine for <i>puru</i> that grows on the feet: take a ripe black or white <i>kecubung</i> . Burn it, then cover it with the male shell. Then, steam the medicine on the affected bare feet; apply the steam as long as the patient can stand the heat. Do this four times consecutively in the morning and in the afternoon, it will heal.			

¹ No mention of *puru parang* in the formulation. However, in Kitab Tib Muzium Terengganu, the author placed the formulation under the section for *puru parang*, thus it is added here.

7	KTMT 036.195.012	<p>Sebagai lagi ubat puru yang mengeluarkan puru parang di dalam tubuhnya tiada mau keluar. Ambil daun urang-aring yang merah taruknya. Maka tumbuk lumat-lumat. Perah ambil airnya. Maka campur dengan kuning telur tiga butil dipecah beri mesra-mesra. Maka beri minum pagi, mujarab insya-Allah Taala, aflat.</p> <p>Another remedy for yaws, take <i>urang-aring</i> leaves of reddish shoot/bud. Pound finely, squeeze it and take its juice. Mix with three egg yolks and beat them. Drink it in the morning, it is therapeutic, if God wills it, it will heal.</p>	<p>Urang-aring</p> <p>Kuning telur</p>	<p><i>Eclipta prostrata</i> (L.) L.</p> <p>Egg yolk</p>	<p>A: Orally taken</p> <p>DG: Drink the remedy in the morning</p>
8	KTMT 036.195.016	<p>Sebagai lagi ubat puru parang baharu hendak tumbuh. Maka ambil terusi tengah tahlil, kunyit sekupang dan mesui sekupang dan air limau nipis lima belas biji. Giling lumat-lumat. Akan airnya limau nipis. Itulah akan airnya, maka mesrakan diberi baik. Maka sapukan kepada puru itu tiga hari. Jangan kena air supaya aflat.</p> <p>Another remedy for newly formed <i>parang</i> yaws, take half <i>tahlil</i> of <i>terusi</i>, a <i>kupang</i> of <i>kunyit</i> and <i>mesui</i> and fifteen <i>biji</i> of <i>limau nipis</i>. Grind everything finely. Mix them with <i>limau nipis</i> juice. Then, apply on the lesion for three consecutive days. Do not let the lesion contact with water to ensure smooth healing.</p>	<p>Terusi</p> <p>Kunyit</p> <p>Mesui</p> <p>Limau nipis</p>	<p>Copper sulphate</p> <p><i>Curcuma longa</i> L.</p> <p><i>Cryptocarya massoy</i> (Oken)</p> <p>Kosterm.</p> <p><i>Citrus aurantifolia</i> (Christm.)</p> <p>Swingle</p>	<p>A: Topical</p> <p>DG: Apply on lesion for 3 consecutive days</p>
9	KTMT 036.195.017	<p>Sebagai lagi ubat daripada Datu Tarab ubat puru restung tumbuh pada leher atau pada lidahnya atau langit-langit pun baik atau puru parang pun baik. Ambil ubat cina sekati. Maka kacip sebahagi. Rebus bahagi dua. Setengah rebus, setengah, taruh airnya sebuyung kira-kira sama bahagi. Maka minum pagi; sentiasa jadikan air minum. Jangan minum air benar lagi. Sudah maka ambil ubat cina setengah kati, diserbuk lumat-lumat. Maka makan dengan air yang setengah itu pagi secawan, petang secawan, apabila sampai empat puluh hari pantangnya maka ambil pula lada sulah secupak, rebus bulat-bulat, maka minum airnya sehari. Adapun selama berpantang empat puluh hari itu akan lauknya ayam betina, aflat.</p> <p>Another remedy from <i>Datu Tarab</i>, <i>puru restung</i> that grows on neck or tongue or palate can heal, and <i>puru parang</i> can also heal. Take one <i>kati</i> of <i>ubat cina</i> and cut into half. Boil them and later divide them into two portions. <i>Setengah rebus, setengah, taruh airnya sebuyung kira-kira sama bahagi</i>. Later, during day time; always make it as drinking water. Do not drink <i>air</i></p>	<p>Ubat cina</p> <p>Lada sulah</p>	<p>No information</p> <p><i>Piper nigrum</i></p>	<p>Orally taken (as decoction and medicine)</p>

benar yet. Once this water is completely consumed, take half kati of ubat cina and pulverize it well. Then, eat it with a cup of the previous divided water in the morning and also a cup in the evening. After 40 days of confinement, take one cupak of lada sulah, boil it and drink the water for one day. During the 40 days of confinement, the patient is only allowed to eat female chicken as the dish.

10 KTMT
036.196.018

Sebagai lagi ubat puru parang segala puru yang besar-besar atau bengkak sendi tulangnya. Inilah akan ubatnya. Pertama tuba tikus dan kemenyan dan belerang bang dan sedelinggam. Sekalian yang tersebut itu sama timbang beratnya. Setelah sudah timbang, kemudian daripada itu pertama ambil tuba tikus sama timbang dan bara tempurung dan sedelinggam setimbang dan bara tempurung setimbang dan belerang bang setimbang. Maka sekalian itu giling lumat-lumat. Jadikan serbuk. Setelah sudah serbuk, maka taruh. Apabila hendak menjual dia, ubat ini berat tujuh emas sekupang harganya. Adapun barang siapa hendak makan dia dudut. Adapun syaratnya mengambil dia jemput dengan tiga jari sekali dudut tiga sehari dudut. Adapun syaratnya bakar bara tempurung, maka ambil tempurung reput di atas, beri reput, maka digoreng tempurung itu, bubuh isinya maka dudutlah. Adapun syaratnya apabila khayal setengah, makan nasi rendang dan pantangnya jangan makan pisang mengkal dan barang yang masam dan ikan yang bias dan yang tiada bersisik jangan dimakan. Apabila makan dia tiga kali sehari, insya-Allah Taala, aflat.

Tuba tikus
Kemenyan

Belerang bang
Sedelinggam
Tempurung

Arsenous acid
Styrax benzoin
Dryand.
Arsenic sulfide
Cinnabar
Cocos nucifera L.

A: Inhalation
DG: Three times
per day

To treat *parang yaws*, any huge lesions, swollen joints and bones. This is the remedy. First, (take) *tuba tikus, kemenyan, belerang bang* and *sedelinggam* of same weight. Then, take *tuba tikus* with coconut shell embers, *sedelinggam* with coconut shell embers, *setimbang* and *belerang bang*. Grind them finely and make into powder. Then, keep it. When it is time to sell it, the remedy should be sold at a price of *sekupang* per seven gold-weighed. When it is going to be consumed, the remedy is consumed through inhalation. The rule is to take the remedy using three fingers, inhaled three times per day. Another rule is to burn the coconut shell and take the broken burned shell and let it crush. The crushed shell is then fried, add in its kernel. After that, inhale it. Another rule, if the patient goes half imaginary, eat *rendang* rice.

11 KTMT 036.197.025	<p>The taboos are <i>mengkal</i> banana, sour food and fish without scales. Eat the remedy three times a day, if God wills it, (it will) heal.</p> <p><i>Sebagai lagi obat puru parang yang merebak tiada mau sembuh. Maka ambil sedelinggam berat enam kupang dan arang tempurung berat enam kupang dan arang cenderung pun enam kupang. Maka diuli lumat-lumat, maka jadikan enam bekas. Maka ambil belanga dua buah sama besarnya keduanya, maka dirapatkan belanga dua buah itu, maka buat lubang belanga itu, maka bubuh bara api dalam belanga itu, maka ambil obat ini, bungkus, masukkan di dalam belanga itu, maka hisap asapnya dengan pendudut. Apabila berhenti maka tutup dengan jari pendudutnya itu; mendudut dia pagi sekali petang sekali. Jika purunya luas sekalipun sembuh olehNya, insya-Allah Taala.</i></p>	Sedelinggam Tempurung Cenderai	Cinnabar Cocos nucifera L. Microcos tomentosa Sm.	A: Inhalation DG: Inhale the remedy once in the morning, once in the evening.
12 MSS1292.1	<p>To treat spreading <i>parang</i> yaws that is hard to heal. Take six <i>kupang</i> of <i>sedelinggam</i>, six <i>kupang</i> of coconut shell charcoal and six <i>kupang</i> of <i>cenderung</i> charcoal. Then, knead well and divide into 6 containers. Take two similar sized <i>belanga</i>, put them closely and make hole inside the <i>belanga</i>. Put embers inside the <i>belanga</i>. The previous remedy is wrapped and put inside the <i>belanga</i>. Inhale the smoke using inhaler. If the patient intends to stop, close the inhaler using his finger. Inhale the smoke once in the morning and once in the evening. If the lesion is so powerful, it will still heal, by God's will.</p> <p><i>Bab pada menyatakan obat puru parang dan lainnya. Fasal pada menyatakan obat parang; akan ubatnya ambil adas tengah tahil jika laki-laki; jika perempuan lima emas beratnya; gula dua tahil, terusi lima kupang, pucuk seemas, manjakani seemas, jintan hitam seemas. Sekaliannya itu disatukan. Maka uli tujuh ari dalam belangan besi; pengulinya pun besi. Setelah genap 7 hari maka rendang beras beri kering, campurkan beri lekat (atau likat) di tangan; maka kelik 14. Setelah sudah maka makan nasi beri kenyang (kenyang; maka makan dua biji), sediakala demikian juga. Tatkala makan obat itu jangan makan nyiur muda dan tebu dan pisang, sekalian yang sejuk jangan di makan. Jika mulut bengkak, kulum halia insyaAllah sembuh. Setelah sudah habis 14 itu, beri bedak dan jangan makan bergaram; dan makan itu jangan mengadap bulan, afiat olehnya.</i></p>	Adas Gula Terusi Pucuk Manjakani Jintan hitam Beras	Foeniculum vulgare Sugar Copper sulphate Saussurea costus (Falc.) Lipsch. Quercus infectoria G. Olivier Nigella sativa L. Oryza sativa L.	A: Orally taken DG: Eaten twice a day for 7 days

A chapter that states about the remedy for *puru parang* and others. About the remedy for *puru parang*; the treatment to it, take a half *tahil* of *adas* (if the patient is a male); while take five *emas* of *adas* (if the patient is a female); two *tahil* of sugar, five *kupang* of *terusi*, an *emas* of *pucuk*, *manjakani* and *jintan hitam*. All of these ingredients are mixed together. Then, knead them for 7 days in a metal container; the kneader is also of metal. After 7 days, roast *beras* till dry, mix it with the kneaded remedy until it sticks to the hand; then roll the remedy into 14 portions. After done making the remedy, then the patient needs to eat until he feels full. Once full, eat two portions of the remedy. During the consumption of the remedy, do not eat young coconut, sugar cane, banana and any 'cold' food. If the mouth gets swollen, mumble ginger and it will heal (with His wills). Give *bedak* and do not eat salty food; and when you consume the remedy, do not face the moon. He (God) will heal it.

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| 13 | MSS1292.2 | <p><i>Sebagai lagi ubat puru parang tumbuh pada tapak kaki. Pertama ambil akar rembega, tunu. Setelah sudah maka rebus dengan air maka bubuh kunyit, getang teguh-teguh maka pasakkan getangnya itu maka keluarkan asapnya, asapkan puru pada tapak kaki atau tangan yang sakit itu, afiat olehnya.</i></p> | <p><i>Rembega</i>
<i>Tunu</i>
<i>Kunyit</i></p> | <p><i>Calotropis gigantea</i> (L.) Dryand
No information
<i>Curcuma longa</i> L.</p> | <p>A: Body steaming</p> |
| <p>Another remedy for <i>parang yaws</i> which grows at sole. Take <i>rembega</i> root and <i>tunu</i>. Then, boil them with water, and add <i>kunyit</i>. <i>Getang teguh-teguh</i> maka pasakkan <i>getangnya itu</i>. Then, once steam is produced, channel it to the sole or painful hand area. (It will) heal.</p> | | | | | |
| 14 | MSS1292.3 | <p><i>Sebagai lagi ubat tangas puru parang. Pertama ambil sedelinggam berat sepaha; jika budak, berat tiga emas, tersi dua emas, belerang dua emas, mustaki berat sekupang. Sekalian itu pipis, bahagi empat belas maka bungkus dengan kertas. Tatkala berasap dia beri makan dahulu; maka bubuh bara api pada suatu tempat maka bubuh ubat itu sebungkus, maka berkelubung dengan kain beri berasap di dalam kelubungnya hingga habis asapnya itu sudah, sekali pagi sekali petang, habiskan empat belas itu hingga tujuh hari demikian juga. Tatkala berasap itu jangan minum air sejuk dan jangan makan ikan yang bisa dan air nyiur, afiat olehnya.</i></p> | <p><i>Sedelinggam</i>
<i>Tersi</i>
<i>Belerang</i>
<i>Mustaki</i></p> | <p><i>Cinnabar</i>
Copper sulphate
Sulphur
<i>Pistacia lentiscus</i> L.</p> | <p>A: Body steaming
DG: Body steaming is done until steam goes off. Repeat for seven days (once in the morning, once in the evening)</p> |

To treat *parang* yaws through steam. Firstly, take a quarter of *sedelinggam*, (if child) use three gold-weighed of *sedelinggam*, two gold-weighed *tersi* and two gold-weighed *belerang* and *sekupang* of *mustaki*. Pound everything and divide them into fourteen portions then wrap using paper. Once the smoke is produced, eat the remedy first. Then, put the ember at a spot and also, put a pouch of the remedy there. Do body steam with the remedy until the steam goes off. Once in the morning and once in the evening. Finish all the 14 pouches by the seventh day. During the body steaming process, do not drink cold water, *bisa* fish and coconut water. (It will) heals.

NB. *Tangas* is a traditional healing method in the Malay culture as a part of body steaming

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| 15 | MSS1292.4 | <i>Sebagai lagi ubat puru parang yang lebar bengkak, ambil timah putih berat sepaha dan timah hitam berat sepaha maka kikir lumat-lumat timah kedua itu. Setelah lumat ambil tuba tikus kadar sekenderi maka campurkan, ramas; sudah mesra maka bahagi enam maka bungkus maka tangaskan, pagi sekali petang sekali, insya Allah taala afiat olehnya.</i> | <i>Timah putih</i>
<i>Timah hitam</i>
<i>Tuba tikus</i> | White tin
Black tin
Arsenous acid | A: Body steaming
DG: Repeat for few days (once in the morning, once in the evening) |
|----|-----------|--|---|---|--|

To treat the broad and swollen *parang* yaws, take a quarter of *timah putih* and a quarter of *timah hitam*. Then, scrub both of them and mix with a *sekenderi* of *tuba tikus*. Squeeze them together and divide into six portions. Once in the morning and once in the evening. If God wills it, it will heal.

Puru dalam tulang

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|---|---------------------|--|--|--|---|
| 16 | KTMT
036.197.022 | <i>Sebagai lagi ubat puru sakit di dalam tulang. Ambil lada tujuh biji dan sunti halia. Maka pipis, airnya air madu dan minyak sapi. Maka ketil, makan dia malam juga.</i> | <i>Lada</i>
<i>Sunti halia</i>
<i>Madu</i>
<i>Minyak sapi</i> | <i>Piper nigrum</i>
<i>Zingiber officinale</i>
Honey
Ghee | A: Orally taken |
| <i>Another remedy for puru that causes pain to the bone. Take 7 lada and sunti halia. Then, pound them and air madu and minyak sapi are used. Make into pellet and eat during night time.</i> | | | | | |
| 17 | KTMT
036.197.024 | <i>Sebagai lagi ubat puru dalam tulang. Ambil air madu sekati dan bawang putih sepuluh tahlil. Maka bubuh dalam air madu itu. Maka taruh baik-baik dalam suatu</i> | <i>Madu</i>
<i>Bawang putih</i> | Honey
<i>Allium sativa</i> | A: Orally taken
DG: prescribed for 10 days, 1 tahlil |

bekas. Maka diketang teguh-teguh barang tujuh hari. Sudah, makan berat setahil sekali makan, aflat.

of medicine per day

Another remedy for *puru* inside the bone. Take a *sekati* of *air madu* and ten *tahil* of garlic. Put them into *air madu*. Properly keep them in a container. Tie them well for 7 days. Later, eat one *tahil* at each meal. He (God) will heal it.

* Formulation numbers for KTMT are based on the numbering in the book by Hussain (2019). KTMT, Kitab Tib Muzium Terengganu

Comparison with scientific studies

The medicinal use of selected materials from the Malay medical manuscripts were compared with contemporary studies. No articles could be found when we first did a search to link the plant materials and *Treponema pallidum* spp. or yaws. However, with the use of broader terms such as antimicrobial, anti-inflammatory and wound healing, a few related journal articles could be found (Table 4).

Table 4: Contemporary use of selected plant-based materials mentioned in the Malay medical manuscripts for the treatment of *ibu puru*, *puru parang* and *puru dalam tulang*. None of the materials listed provide evidence against *Treponema pertenuae*, the causal agent for yaws.

No.	Malay vernacular name	Scientific name	Prescription in the Malay medical manuscripts	Medicinal effects	Study method [§]	Reference
1	<i>Adas</i>	<i>Foeniculum vulgare</i>	An ingredient in the oral medicine that treats <i>puru parang</i>	Anti-inflammatory and antimicrobial activities of fenchone and limonene oil, the two compounds of <i>F. vulgare</i> , increased collagen synthesis and decreased the number of inflammatory cells during wound healing and may be useful for treating skin wounds. Compiled data indicate efficacy of <i>F. vulgare</i> in pharmacological properties such as antibacterial, anti-inflammatory, antinociceptive and antioxidant.	Excisional cutaneous wound in rats model	(Keskin et al., 2017)

					<i>In vitro</i> and <i>in vivo</i> studies	Reviewed by (Badgujar, Patel, & Bandivdekar, 2014) (Ampawong et al., 2020)
2	Beras	<i>Rice, Oryza sativa</i> L.	Used topically as after-bath talcum powder or lotion to treat <i>puru parang</i> . Also orally taken with other ingredients to treat <i>puru parang</i> .	Rice extract (topical cream-based for rats) was found to reduce epidermal inflammation, increase the expression levels of anti-inflammatory cytokines (IL-10 and TGF- β), reduce the levels of pro-inflammatory cytokines and enhance the antioxidative property (Nrf-2)	Human psoriatic artificial skin; an imiquimod-induced rat psoriasis model	
3	Jintan hitam	<i>Nigella sativa</i> L.	Orally taken with other ingredients to treat <i>puru parang</i> .	Both oral and topical thymoquinone reduced the inflammatory cells infiltration in the blood. Nigella and Betamethasone showed significantly more rapid improvement in hand eczema compared with Eucerin; Nigella ointments improves life quality compared with Eucerin. Thymoquinone, a compound of <i>N. sativa</i> , has anti-inflammatory, antioxidant, and antibacterial properties, which mainly contributed to wound healing process.	Atopic dermatitis mice model RCT double-blinded clinical trial in new cases of hand eczema with 18-60 years of age Animal models	(Aslam, Shahzad, Shabbir, & Irshad, 2018) (Yousefi et al., 2013) Reviewed by (Sallehuddin, Nordin, Bt Hj Idrus, & Fauzi, 2020)

4	Kunyit	<i>Curcuma longa</i> L.	An ingredient for body steaming to treat <i>puru parang</i> .	Water extract <i>C. longa</i> (WEC) has anti-inflammatory effects and augments hyaluronan production in the skin Clinical trials suggest that WEC tablets may be useful for randomised facial skin.	In vitro ultraviolet B-irradiated keratinocytes RCT, double-blind, placebo-controlled trial	(Asada, Ohara, Muroyama, Yamamoto, & Murosaki, 2019)
5	Manjakani	<i>Quercus infectoria</i> G. Olivier	To treat <i>puru parang</i> . Can also be used to treat swollen mouth and tumour.	Topical <i>Quercus infectoria</i> formulations exhibited antibacterial and antioxidant activities, and enhance the wound healing process in diabetic rats with abundant cellular infiltration, collagen deposition, and re-epithelialisation	Streptozotocin-induced diabetic rats	(Chokpaisarn, Chusri, Amnuakit, Udomuksorn, & Voravuthikunchai, 2017)
6	Nyiur (tempurung)	<i>Cocos nucifera</i> L. (coconut shell)	To treat <i>puru</i> in general, as well as persistent <i>puru parang</i> , <i>puru</i> with big lesions, lesions on soles, swollen joints Also can be used as antimicrobial agent against <i>puru</i> pathogens and as wound healing agent.	Topical application of coconut shell liquid smoke promotes burn wound healing possibly by increasing the number of fibroblasts. Distilled liquid smoke (DLS) derived from coconut shell was investigated on a traumatic ulcer with the diabetic rat. Topical application of DLS increased the amount of skin collagen. Coconut oil in dermatologic skin demonstrated antioxidant, anti-inflammatory and anti-itching properties.	Burn wound animal model Diabetic-induced rat model	(Tarawan, Mantilidewi, Dhini, Radhiyanti, & Sutedja, 2017) (Surboyoy, Arundina, Rahayu, Mansur, & Bramantoro, 2019) Reviewed by Vaughn 2018, Deen 2021, Poljsak 2020

	Pucuk	<i>Saussurea costus</i> (Falc.) Lipsch.	Orally taken with other ingredients to treat <i>puru parang</i>	Extracts of <i>Saussurea costus</i> (SC) and <i>Thuja orientalis</i> L. (TOL) were found to decrease the expression of protease-activated receptor-2 and ICAM-1 and the release of TNF- α and IL-6 in HaCaT cells, when applied topically for 5 weeks. SC+TOL treatment decreased the inflammatory cellular infiltrate, in comparison to either of SC or TOL	Various in vitro and animal studies HaCaT cells and the dorsal skin of Nc/Nga mice had a local exposure of house mite extracts and 2,4-dinitrochlorobenzene (DNCB), respectively.	(Yang et al., 2017)
	Rembega	<i>Calotropis gigantea</i> (L.) Dryand	Water boiled extraction of <i>rembega</i> is used to make remedy for body steaming	Ethanollic and aqueous extracts at dose of 200 mg/kg showed potent anti-inflammatory activity at the end of 3 h	Carrageen induced paw oedema models	Reviewed by (Kadiyala, Ponnusankar, & Elango, 2013)
7	Sirih	<i>Piper betle</i> L.	To treat <i>ibu puru</i> and <i>puru parang</i> . Also as an antipruritic agent.	A variety of decoctions to cure numerous skin problems including wounds, urticaria, burns, eczema. A paste of <i>P. betle</i> leaves is applied on cuts and wounds or mixed with salt and hot water to treat filariasis. The leaves can also be applied locally to cure inflammatory swelling. Leaf preparations and the leaf sap are applied to wounds, ulcers and boils.	Animal models	Reviewed by (Salehi et al., 2019)
8	Urang-aring	<i>Eclipta prostrata</i> (L.) L.	An ingredient to make oral medicine for <i>puru dalam tulang</i> .	Anti-inflammatory activity revealed that <i>E. prostrata</i> compounds inhibited nitric oxide production in lipopolysaccharide-stimulated RAW264.7 cells.	In vitro study using murine macrophage-like RAW264.7 cells	(Le et al., 2021)

[§]RCT, randomised controlled trials

Discussion

Remedies for *puru* have been documented in Malay manuscripts, a form of handwritten documents in Malay language (*Jawi* script) whereby manuscripts which discuss medicine are referred to as Malay medical manuscripts or *Kitab Tib*. In ancient Malay manuscripts, *puru* is a general term for various types of skin diseases, including ulcers, sores and yaws. In Gimlette (1939) alone, there are more than 20 types of *puru* listed, but only 19 could be associated with yaws. An exploration on the remedies and treatment from the Malay medical manuscripts can offer solutions to yaws eradication in tropical countries. Yaws is one of the neglected tropical diseases defined by the WHO. It is highly prevalent and endemic in certain countries, and without early treatment, patients may be left with life-long deformities and disabilities. This can cause a significant burden of morbidity, mortality, suffering and economic loss. Patients may be left with life-long deformities and disabilities.

Based on the terms from Gimlette (1939), and the occurrence of the terms *ibu puru*, *puru parang* and *puru dalam tulang* in KTMT and MSS1292, we shortlisted 17 formulations as those which could potentially be the treatment for yaws (Table 2). The authors would like to reiterate that it cannot be confirmed as to whether these formulations are in fact, effective against yaws, or against any pathogens, and further laboratory study should be carried out to test the active ingredients against human pathogens. Nevertheless, these formulations shortlisted as the potential treatment against yaws, demonstrated the richness of the Malay medicine in terms of the materials used in the traditional medicine and the variety in the methods of administration (i.e. topical application, body steaming, inhalation technique and bath remedy are amongst the treatment for the disease).

The number of remedies for *puru parang* is higher than for the other yaw-related *puru*.

Literature search using scientific databases could not retrieve studies that treated yaws using natural plants prescribed by the Malay medical manuscripts. However, most of the plants mentioned in the Malay medical manuscripts exhibit anti-inflammatory and wound healing properties, which complement the treatment for yaws. Table 4 summarises selected findings from scientific literatures that support the use of these plants as the traditional medicine to treat yaws-related skin lesions, based on lesion-induced animal models as well as randomised controlled clinical trials. In the current scientific literatures, many empirical studies to support the use of natural plants or traditional plants and materials tend to conduct their experiments using single materials (mono-ingredient), or by extracting the bioactive compounds. This could reduce the medicinal potential of the traditional formulations.

Conclusion

The findings from this study suggest that in general, the information and knowledge of *puru* treatment in the Malay medical manuscripts are comprehensive with a clear and understandable description of formulations, method of preparations and method of administrations to the treatment. The use of natural products as remedies for yaws would benefit low-income countries towards the development of cost-effective treatment to curb the spread of endemic yaws. The contemporary studies related to the medicinal values of the materials prescribed in the manuscripts demonstrate that there is significant evidence on their roles in treating skin lesions. Comparative analysis found that there were no reports on the use of these materials as yaws treatment which open up a huge potential for medical research using manuscript data for the treatment of yaws. The use of these formulations to treat yaws or any other skin diseases can only be warranted after vigorous laboratory experiments and clinical trials to evaluate their therapeutic efficacies.

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