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## Understanding cancer and its treatment in Thai traditional medicine: An ethnopharmacological-anthropological investigation

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### Abstract

*Ethnopharmacological relevance:* Thai traditional medicine (TTM) is widely practiced in Thailand and continues to gain importance in cancer management, but little is known about the TTM practitioners' emic concepts and practice.

*Aim of the study:* With this study we firstly aim to document the practice of cancer treatment and prevention by TTM practitioners and, secondly, to evaluate how such traditional concepts and practices are correlated with biomedical ones. This in turn can form the basis for developing novel strategies for designing pharmacological experiments and longer term strategies to develop TTM practice.

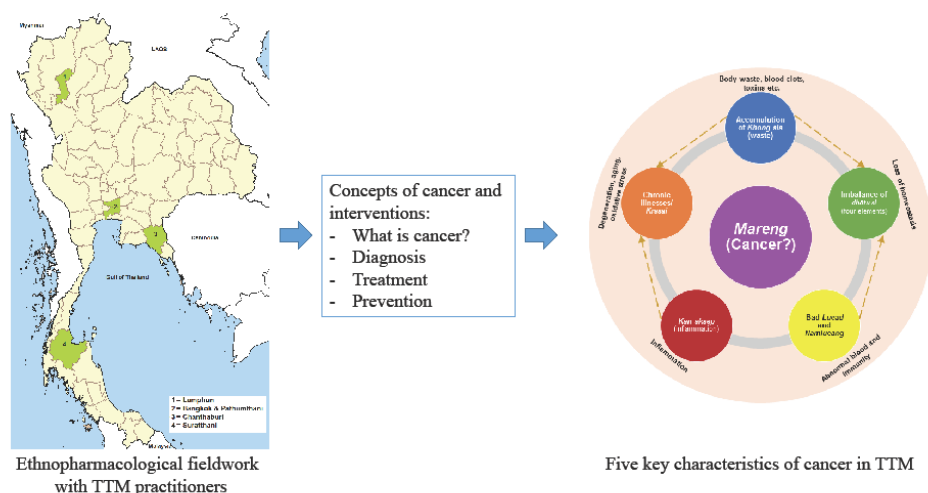
*Methods:* Semi-structured interviews with 33 TTM practitioners were performed in five provinces in different regions of Thailand. The following information were recorded; basic information of informants, descriptions of cancer (*mareng* in Thai), causes, diagnosis, treatment, and prevention. Plants used in the treatment and prevention of *mareng* were also collected.

*Results:* Using an in depth ethnographic approach four representative case studies to assist in a better understanding of the characteristics of *mareng*, its diagnosis, treatment, and prevention are reported here. Five characteristics of *mareng* - waste accumulation (*khong sia*), chronic illnesses (*krasai*), inflammation (*kan aksep*), bad blood (*luead*) and lymph (*namlueang*), and the imbalance of four basic elements (*dhātu si*) - have been identified. Explanatory models of cancer in TTM were linked with biomedical concepts and relevant pharmacological actions. Traditional uses and available scientific evidence of medicinal plants mentioned in the case studies for the treatment or prevention of *mareng* are presented and discussed.

*Conclusion:* Here for the first time five main characteristics of cancer based on Thai traditional medical concepts are analysed. Our findings are relevant not only for the planning of clinical studies or pharmacological experiment in the search for novel compounds for

cancer treatment and prevention, but also for the integration of Thai traditional medicine in cancer care.

## Graphical Abstract



**Keywords** traditional medicine, cancer, integrative medicine, Thai traditional medicine, mareng,

## 1. Introduction

The development of anti-cancer agents has greatly relied on natural products as more than 60% of the available cancer drugs are developed from natural sources. For instance, the best known examples include paclitaxel from *Taxus brevifolia* Nutt. (Taxaceae), vincristine and vinblastine from *Catharanthus roseus* (L.) G.Don (Apocynaceae), and etoposide which is a derivative of podophyllotoxin from *Podophyllum peltatum* L. (Berberidaceae) (Gordaliza, 2007; Heinrich, 2010).

Such discoveries have often been linked to ethnopharmacological research. Among all natural sources, plants in traditional medical systems have been reported most often to be used in cancer management. However, their uses against cancer may in fact suffer from a poor understanding of the underlying traditional medical concepts (Jacobo Herrera et al.,

2016). This calls for a systematic assessment of ‘what is cancer?’ in the context of a traditional medical system and how this may be linked to biomedical research, generally preclinical research. Thai Traditional Medicine (TTM) offers an opportunity to explore this dichotomy. Not only has it developed a systematic conceptual basis, but it is also well embedded in Thai culture, which has been transmitted over centuries and today it is developing into an essential element of health care in Thailand.

TTM is a health care system, which is based on Buddhism and – according to self-recognition - is in harmony with Thai culture. Various forms of practice - namely herbal medicine, massage, midwifery, maternal and child healthcare, Buddhist rites, and other rituals based on the belief in supernatural power- are practiced in the system (Chokevivat and Chuthaputti, 2005). It is considered a holistic medical system. According to its theory, the human body is composed of four elements (*dhātu*): Earth (*dhātu din*), water (*dhātu nam*), wind (*dhātu lom*), and fire (*dhātu fai*). Health problems are caused by the imbalance of these elements (Saralamp et al., 1996). In the past decades, it has gained importance especially in chronic diseases, including chronic pain and cancers. Although scientific evidence to support the use of Thai traditional drugs in cancer is lacking, medical experience and anecdotal accounts of the benefits of TTM against the disease are well known throughout Thailand. However, little systematic information is available about the knowledge and practice of TTM practitioners regarding ‘cancer’.

Currently no statistical data on TTM use by cancer patients in Thailand is available. Several studies showed that after their cancer diagnosis around 40-60% of cancer patients in Thailand have used non-biomedical forms of treatment, including traditional medicines. Chinese and Thai medicinal plants are the most common herbal medicine used by these patients. The surveys reported that the patients benefited from such therapies, especially recording an improvement in the quality of life (Poonthananiwatkul et al., 2015; Puataweepong et al., 2012).

In TTM, as well as other traditional medical systems, diagnosis is based on observation and interpretation of patients’ symptoms, suffering, past history, causes, effects, and responses, mostly without objective information. On the other hand, in biomedicine, diagnosis relies on objective physical examinations together with patient's history and pathophysiology information obtained from laboratory. This results in a cultural gap between the two systems (Berger-González et al., 2016). To bridge this gap, the ‘emic-etic concept’ can be applied. The anthropological terms emic and etic were originally coined in the context of linguistic research by Kenneth Pike in 1954. According to Pike “The etic viewpoint studies behaviour as from outside of a particular system, and as an essential initial approach to an alien system. The emic viewpoint results from studying behaviour as from inside the system.” (Pike, 1967).

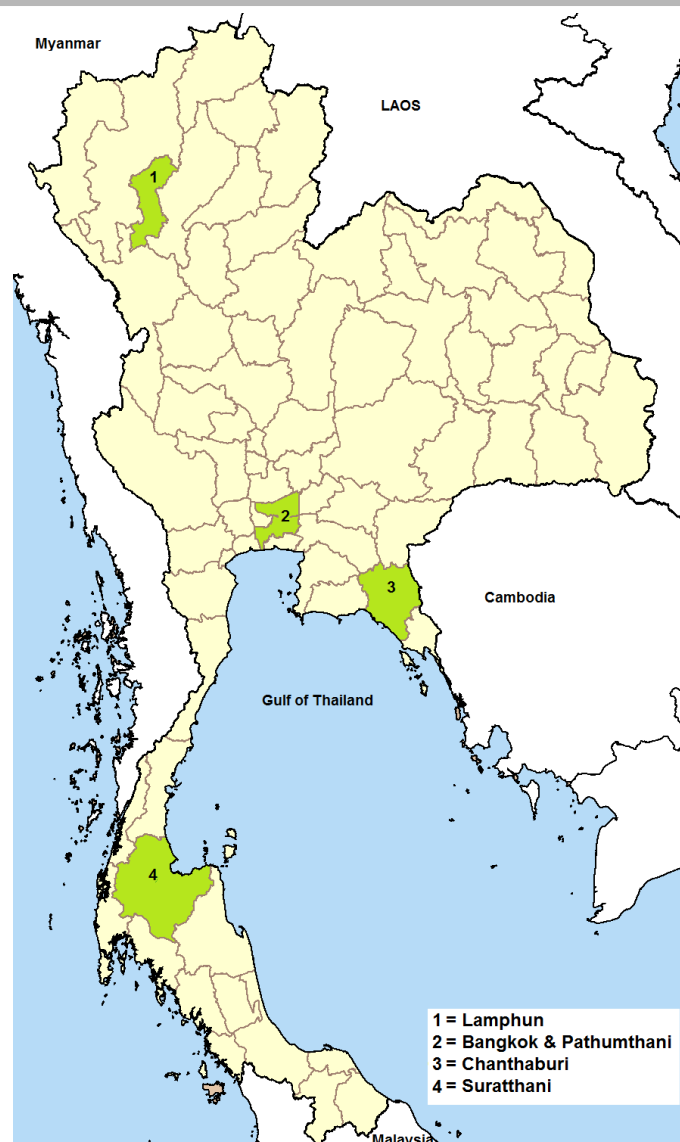
While the ultimate aim of the overarching project is to contribute to the discovery of novel extracts or lead compounds for anti-cancer and chemopreventive agents, the primary objectives of this research are (i) using an in depth ethnographic approach to understand the emic perspective of cancer in TTM, (ii) to provide etic perspective on the species used in these treatments, and (iii) to understand how this impacts on the treatment given by TTM practitioners.

## 2. Methods

Interviews with 33 traditional practitioners in five provinces in different regions of Thailand (Fig. 1), namely Lamphun (northern); Suratthani (southern); Chanthaburi (eastern); and Bangkok, Nonthaburi, and Pathumthani (central), were carried out during December 2013 – April 2014. The practitioners’ names and locations were obtained from the Center of Applied

Thai traditional Medicine (Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand), local hospitals, villagers, and other practitioners.

Using an interview guide defining the main questions (Table 1), the interviews were conducted in an open style in informal settings, such as at practitioners' houses. All interviews were performed in Thai. The word '*mareng*' was used in the interviews when referring to cancer. Informed consent and a permission to record the conversation were obtained prior to each interview. The medical terms used in this report were translated to English in two steps; from Thai traditional medical terms to modern Thai, and then from modern Thai to English. Plant voucher specimens were collected and deposited at Faculty of Pharmacy, Mahidol University, Bangkok, Thailand (Table 2). Common species (i.e. green mung bean - *Vigna radiata* (L.) R.Wilczek] and marketed herbal products [i.e. *Triphala* – generally considered to contain *Phyllanthus emblica* L., *Terminalia bellirica* (Gaertn.) Roxb. and *Terminalia chebula* Retz.] were not collected. Dried herbal materials were collected in case that the informants could not provide fresh plants (included in Table 3). The taxonomic validation of the species is based on <http://mpns.kew.org/mpns-portal/> and [www.theplantlist.org](http://www.theplantlist.org).



**Fig. 1.** Interview locations in green colour. (Map modified from (Ahoerstemeier, 2004))

**Table 1**

Questions used in the interviews (interview guide).

Required information	Questions used
Informants' perception of cancer and causes	<ul style="list-style-type: none"> <li>What is <i>mareng</i>?</li> <li>What are the causes of <i>mareng</i>?</li> </ul>
Cancer diagnosis by TTM practitioners	<ul style="list-style-type: none"> <li>How do you know that somebody has <i>mareng</i>?</li> <li>Please describe how do you diagnose or identify <i>mareng</i>.</li> <li>What are the main symptoms?</li> </ul>
Cancer treatment	<ul style="list-style-type: none"> <li>How often do you treat <i>mareng</i> patients?</li> <li>Which methods do you use to treat it?</li> <li>What are the dosage regimens?</li> </ul>

	<ul style="list-style-type: none"> <li>▪ How long did/does the remedy take to make patients feel better?</li> <li>▪ What is the theory or treatment concept of <i>mareng</i>?</li> </ul>
Cancer prevention	<ul style="list-style-type: none"> <li>▪ Can <i>mareng</i> be prevented?</li> <li>▪ How can we prevent it?</li> </ul>

The project was approved by the UCL Research Ethics Committee, Project ID: 5068/001, and Siriraj Institutional Review Board (Thailand), Protocol number 779/2556(EC4). All data were collected and stored in accordance with the Data Protection Act 1998.

### 3. Results and discussion

‘*Mareng*’ in modern Thai is the direct equivalent of cancer. It is believed that the word is derived from ‘merengsa’ in Melayu which means untreatable ulcer. However, it is also used to refer to other diseases in TTM scriptures, which might or might not be cancer in a biomedical sense. In this study, the term ‘*mareng*’ was used when referring to a disease in TTM, which might or might not be the same as cancer, and cancer was used only when referring to a biomedical concept or diagnosis.

#### 3.1 *Mareng as a disease*

As the informants had various views on *mareng*, case studies were found to be the best way to represent their knowledge/perception on causes, treatment, and prevention of *mareng*. They contain both informants’ existing knowledge about *mareng* and some examples of past/current cases. A short portrait of each informant is also included.

##### 3.1.1 Case studies

*Informant A – mareng is linked with inflammation (kan aksep), blood circulation, chronic conditions, microorganisms (chuea rok), and chemicals*

Informant A, 53 years old from Pathumthani, studied TTM from a TTM school and graduated with a Bachelor in TTM. Later she also studied Thai traditional massage. She has experience in TTM for around 10 years. Before running her own clinic, she used to work for a clinic where, as she said, ‘cancer patients were the majority because the place was famous in cancer care’. She herself produces herbal medicine with the formulations obtained from ancient Thai medical scriptures. Her father is also a TTM practitioner.

“In general, *mareng* is caused by internal inflammation (*kan aksep*) and microorganisms (*chuea rok*). These microorganisms (*chuea rok*) cause wounds or abscesses in the lungs or the liver. When the body cannot fix it or we intake toxins, the wounds will be bigger and distribute to lymph nodes, and then to other organs. In summary, if we have a chronic condition and our body cannot fix it, that condition will become *mareng*.

*Mareng* in the breast is caused by an obstruction of blood (*luead*) and *lom*<sup>1</sup>. In the early stage, we find hard lumps, pain in the arms, and headaches. Once there is

<sup>1</sup> Lom is an abnormal state that causes symptoms, such as swellings, aching, pains, pressure, and etc. It has a close relation with blood and can distribute to other parts of the body with blood (see Brun and Schumacher, 1994: p. 61).

the obstruction of blood, *phangphued* (can be compared to fibrosis) forms and grows bigger if we don't treat it. If the obstruction continues, waste will accumulate locally. When the microorganisms (*chuea rok*) or chemicals get inside, *mareng* will develop. For the treatment, I use herbal remedies which help improving blood circulation, eliminate *phangphued*, and detoxify the chemicals and the microorganisms. The recipe for *phangphued* comprises *thaowanpriang* (*Derris scandens*), *khokhlan* (*Mallotus repandus*), *phimsen* (borneol camphor), and *karabun* (camphor). The patients will defecate every day to remove the waste. Normally after a month, the lumps will be softer and smaller, and will eventually disappear.

I've also treated a case with lung cancer. The patient has received chemotherapy for 14 times before started TTM therapy with me. I've prescribed a detoxifying remedy for the first seven days to wash away chemotherapy. It can be noticed that the patient's face was brighter and he was less tired, could eat, and had less chest pain. Then I prescribed medicine to treat lung diseases and kill *mareng*.

For *mareng* in the colon, patients will start with detoxifying remedy for three days. Then they will be prescribed *mareng* remedy together with ulcer treatment. I also have to treat other symptoms, such as diarrhoea, indigestion, flatulence, constipation, and bulging stomach which are common co-symptoms of *mareng* in the colon.

In general, *mareng* patients must take medicine that adjust the elements and remove waste, together with *mareng* remedy. Herbs for *mareng* cannot be hot, but it also depends on the type of abnormal elements. I have only one *mareng* remedy for which the main ingredients are *kammathandaeng* (arsenic disulphide), *kammathanlueang* (sulphur), *khaoyennuea* (*Smilax corbularia*), *khaoyentai* (*S. glabra*), *khanthongphayabat* (*Suregada multiflora*), *horathaosunak* (*Balanophora abbreviate*), *khanunsampalo* (*Artocarpus altilis*), and *makhampom* (*Phyllanthus emblica*). I will add other related remedies, such as liver remedies for patients with *mareng* in the liver. Moreover, I will also add massage to facilitate the blood circulation which benefits the treatment because it pushes the medicine and immunity into tumours. The most important thing is to remove accumulated toxins and waste.

To prevent *mareng*, we have to remove toxins daily because we intake them with food. *Mareng* prevention can also be personalised. For instance, patients with chronic gastric ulcer should take herbal medicine that heals wound in the stomach and intestine and detoxifies. Detoxification is the most important step. Also we have to eat properly; like eat balanced diet (e.g. five portions of fruit and vegetables), and avoid food that cause *mareng*, such as internal organs; processed food, eg. sausages; and bamboo shoots."

*Informant B – mareng is linked to the imbalance of elements and chronic conditions (krasai)*

Informant B, 53 years old from Nonthaburi, learned the practice from his aunt. The knowledge has been passed down from generations to generations in his family. He became his aunt's successor in the family's Thai traditional medical clinic. Since he was a child he has helped his aunt in their pharmacy. Before he took his aunt's place, he studied the clinical practice beside his aunt for many years. Now he has been treating patients for more than 10 years.



“In TTM, a disease happens because of abnormal *tridosha*<sup>2</sup>. To treat a disease, we have to re-balance *tridosha* and then the earth element will become normal. Every disease is treated like this, including *mareng*.

*Mareng* is a familial condition that makes a person having an abnormal organ from the beginning. So this kind of disease cannot be prevented because it is already in the blood. However, we could suppress its emergence by preventing *krasai*. A person can develop *krasai* when he/she has a chronic condition. A general method to prevent *krasai* is to eat green mung beans boiled with *rangchued* (*Thunbergia laurifolia*), *triphala*<sup>3</sup>, and sugar. This is a gentle way to wash away poisons to prevent *krasai* with the aim to prevent *mareng*.

An example of *mareng* diagnosis is a patient whom visited me last week with creamy white vaginal discharge during the menstrual cycle. I performed an examination (touching) and could feel lumps in her cervix. Together with other symptoms, I suspected *mareng* in the uterus. So I asked this patient to check up with the hospital (at the time of the interview we did not know the result yet). The most important symptom which led to *mareng* diagnosis in this case was the history that the patient has had abnormal vaginal discharge during the menstrual cycle and dysmenorrhea for a long time. I did not tell her that I suspected *mareng* because she would not believe me.

A case where I have suggested *mareng* prevention is a friend of mine who has a familial history of liver diseases. His parent had liver cancer and his brother died because of a liver disease. I knew that he would develop a liver disease in the future. So I recommended him to take care of the liver by having a diet that good for the liver and taking a liver remedy every 2 weeks. I also check the signs of liver diseases, such as tiredness, feeling sleepy, not eating, flatulence, and white tongue. If he has these signs, liver remedy will be prescribed immediately. For the food, he should not eat spicy food and try to eat bitter food more. He also had to take a remedy to wash away poisons in the blood every three months to prevent a precipitation in the blood (*luead*) and *namlueang*. Furthermore, he has to take a herbal recipe called ‘*Ya-klom-nang-non*’ to nourish the liver for one week every month.

For lung cancer treatment, I will start with a detoxification of the lung. The medicinal plants have to be those that get into the lungs, such as *yamornoi* (*Cyathium cinereum*) and edible bird nests. When I treat cancer patients, I always tell them to use my prescribed herbal medicines together with conventional treatment, but do not tell their doctors otherwise they will be asked to stop herbal remedies. I prefer to use both together because each has its advantages. Herbal medicine alone might not be fast enough to kill the tumours. Conventional treatment is very fast for this purpose. For patients who are taking chemotherapy, I have to prescribe nourishment because their bodies will be very weak.”

*Informant C – mareng is linked with inflammation (kan aksep), fire element, abnormal namlueang, and chronic bruises*

<sup>2</sup> *Tridosha* is the term used to call three elements; *vata*, *pitta*, and *semha* (or *kapha* in Ayurveda), together. It contributes to all major function of the body and a healthy state is a result of the harmony of *tridosha*. More information can be read in The Tridosha Theory by Pal, M. (Anc Sci Life. 1991 Jan;10(3):144-55.).

<sup>3</sup> *Triphala* is a famous TTM herbal medicine which comprises fruits from *Phyllanthus emblica*, *Terminalia bellirica*, and *Terminalia chebula*.

Informant C, 52 years old from Chanthaburi, has practiced TTM for 28 years. When she was young, she always went with her uncle, who was a TTM practitioner, to treat patients. She decided to become a TTM practitioner when she was 16 years old.

“*Mareng* is caused by a severe inflammation (*kan aksep*). The fire element is fully activated. There are two conditions that cause *mareng*. One is from abnormal *namlueang* which is caused by over-activated fire element. The second one is from a chronic bruise. A blood clot that has deposited for a long time could develop to *mareng*.

I have experience in treating *mareng* in the breast. The remedy comprises drugs for *namlueang* conditions, including *khaoyen* (a combination of *khaoyennuea* and *khaoyentai* from *Smilax spp.*), *huayang* (*Smilax ovalifolia*), *nontaiyak* (*Stemona tuberosa*), *kammathanlueang* (sulphur), and a charcoal. Patients have to stop using this medicine once they have recovered because this drug affects neurological system. Some patients took three pots and they recovered.

*Mareng* could be prevented by changing habits; no stress. Fruits and vegetables which have cooling effects (they have ‘cold taste’ in TTM) can help because *mareng* is related to fire element.”

Informant D – *mareng* is linked with chemicals and chronic *mahok*.

Informant D, 74 years old from Lamphun, is a Lanna healer. Lanna medicine is practiced widely by TTM practitioners in the North of Thailand. He obtained the knowledge from his ancestors and also from a famous master in the area. He has had his license for TTM practice for more than 20 years.

“*Mareng* is caused by *lom saan*<sup>4</sup> or *lom khaan*<sup>5</sup>. My master said that smoking causes *khaan* to eat liver and lungs. *Mareng* in the liver is caused by *khaan* eating liver. The cause of *mareng* is food, such as vegetables contaminated with chemicals. Long term *mahok*<sup>6</sup> could develop into *mareng*. Patients who have *lom khaan* will have pains. There are several *khaan*; some cause pale faces or yellow or thin.

Patients with *mareng* in the liver have yellow skin and vomit after eating. I treat them by asking them to drink *nammon* (holy water) and *rangchued* (*T.laurifolia*) drink or *phakhaotong* (*Houttuynia cordata*) drink or a decoction of *kasalong* (*Millingtonia hortensis*), *oidam* (sugar cane), and *yapakhwai* (*Dactyloctenium aegyptium*).

Patients with *mareng* in the intestine have stomach pain, twisted intestine, gas, and flatulence, which are similar with *mahok* in the intestine. The treatment is drinking holy water and a decoction of *kasalong* (*M.hortensis*), sugar cane, and *yapakhwai* (*D.aegyptium*).

<sup>4</sup> *Saan* is a group of diseases that tumours or hard nodules are common characteristics. The accompanying wind that causes *saan* is called *lom saan* (please see Brun and Schumacher (1994) p.135).

<sup>5</sup> *Khaan* is considered the mother of all diseases because it can develop into many diseases (please see Brun and Schumacher (1994) p.100).

<sup>6</sup> *Mahok* (or *bahoog*) is a group of intestinal diseases that twisting pains in lower abdomen, back aches, abnormal faeces, and emaciation are common symptoms ((please see Brun and Schumacher (1994) p.108).

To prevent from a disease, we could drink a decoction from *rangchued* (*T.laurifolia*) and rice, or a combination of *kasalong* (*M.hortensis*)-sugar cane-yapakkhwai (*D.aegyptium*), or have an herbal steam bath.”

### 3.2 Disease explanation of cancer in Thai traditional medicine

Generally, *mareng* is classed as a disease which develops when there is chronic *fi* (abscesses), untreated chronic conditions, spoiled *luead* and *namlueang*, *kan aksep* (inflammation), or chronic bruises. Some informants also stated that *mareng* is any fast progressive diseases or body/organ degeneration. This is similar to the definition of cancer from traditional healers in other medical systems like in Malaysia who define cancer as a prolonged sickness or accumulation of abscesses (Al Naggar et al., 2012) and Guatemala (Maya) where cancer is seen a disease that is difficult to treat (Berger-González et al., 2016). Traditional healers in Nigeria and Navajos also associated cancer with an ulcer that does not heal easily (Csordas, 1989; Nwoga, 1994). This may point to one common characteristic of traditional medical systems: traditional practitioners have no modern equipment for physical examination. As a result, abscesses and wounds are among the symptoms that can be seen and can be compared to ancient texts.

Since the practitioners do not have any tools that help in diagnosis or confirmation of cancerous cells, the diagnosis relies on patients' symptoms and their history, especially the history of cancer in the family, eating habits, and their work situation. The practitioners recognise that cancer is a disease in Western medicine. Since most patients were already diagnosed with cancer prior to the visits, the practitioners did not diagnose them again. However, the informants had to check patients' *dhātu* and symptoms using TTM diagnostic approaches in order to prescribe suitable treatments. Sometimes they compared the symptoms, mostly nodules and *fi*, with old texts. One informant uses spiritual diagnosis called *Pheng Kasin* in which he invites the patient's spirit to come and give the information about the sickness. Two informants checked the pulse as they said cancer patients have a very fast pulse with a specific pattern. This is a method used in Traditional Chinese medicine (TCM). These two informants have studied both TTM and TCM and they prescribe both Chinese herbs and Thai herbs.

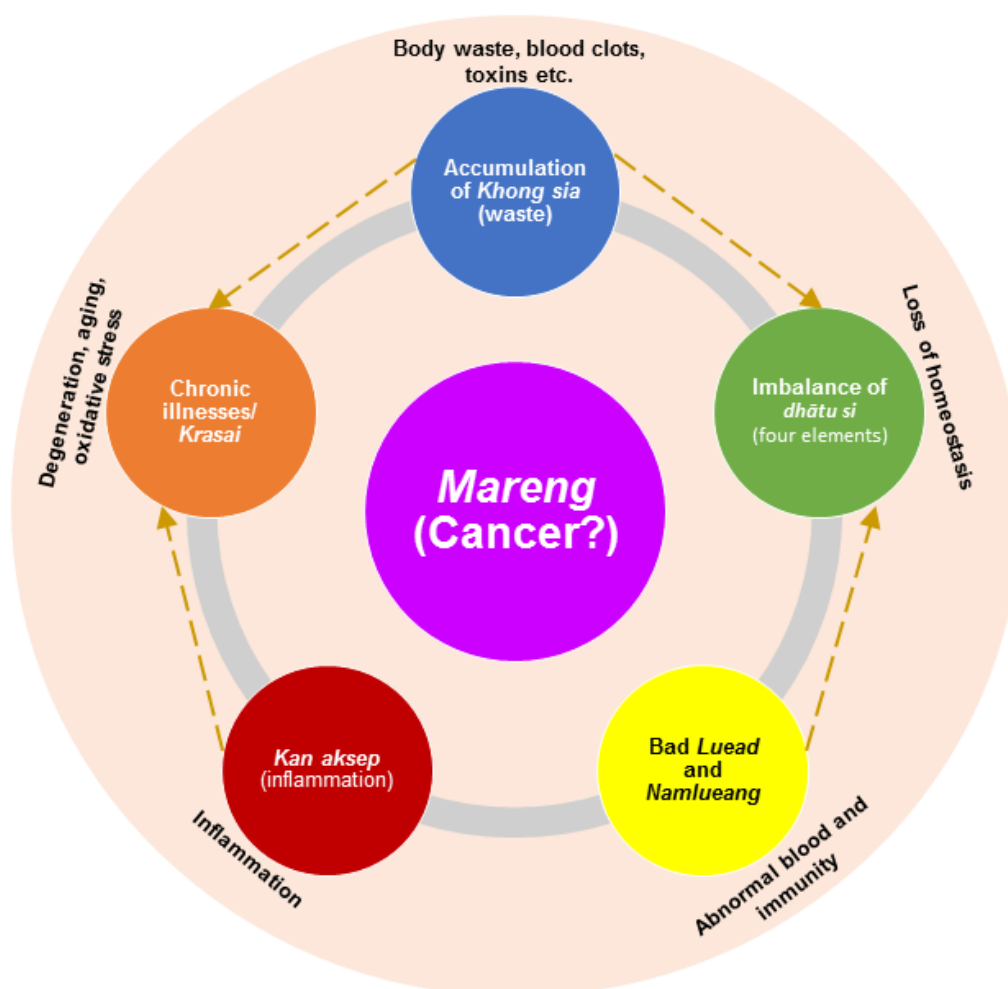
Based on the informants' responses, causes of *mareng* can be divided into internal and external factors. External factors are factors that a person is exposed to in the environment which include food, chemicals, *phayat*, *tua*, tobacco, and sunlight. *Tua* is generally used to classify 'living things with legs' and *phayat* means illnesses or parasites. Thai people use these words to refer to living things. Consequently, some informants viewed *mareng* as a living entity (Bamber, 1987). Interestingly, this is similar to Maya healers who stated that cancer is moving within the body (Berger-González et al., 2016). In essence these are emic concepts, and also some perceived causes are in agreement with current knowledge that smoking, fried food, red meat, sunlight, and pollutants cause cancer (Anand et al., 2008).

Internal factors are linked to modern concepts. These include genetics and conditions that develop within the body and affect four basic elements (*dhātu si*), such as chronic abscesses, serious inflammations, degeneration of the body or organs, and an 'unhealthy immune system'.

### 3.3 Linking explanatory models of cancer in Thai traditional medicine with biomedical concepts

Understanding characteristics of *mareng* from an etic perspective helps in a better understanding of the actions of *mareng* treatments in TTM. The case studies above are

representative of informants' different perceptions of *mareng* which covered five main characteristics of *mareng* (Fig. 2). These characteristics - waste accumulation (*khong sia*), chronic illnesses/*krasai*, inflammation (*kan aksep*), bad *luead* and *namlueang*, and imbalance of four basic elements (*dhātu si*) - were found to be common in patients who suffered from *mareng* and the treatments were based on this classification. The main characteristics here are our interpretation based on interviews with 33 TTM practitioners (our etic perspective). They are based on the description of *mareng*, causes of *mareng*, and its treatment and prevention. For some topics, some species used (this is etic perspective) provide examples of how *mareng* is treated (Table 2). Since this is an ethnographic approach in different regions, a quantification of uses was not included. The species highlighted are those which are more commonly known and which could be identified to genus level during the research (cf. Table 3 for species with a tentative identification).



**Fig. 2.** Main characteristics of cancer based on TTM practitioners' perspectives. The arrows show the relationships between each characteristic. Inflammation (*kan aksep*) and accumulative waste cause *krasai*. Accumulation of waste and bad *luead* and *namlueang* cause the imbalance of *dhātu si*. The outer circle shows a matching of each TTM concept with possible Western medical ones.

### 3.3.1 *Luead sia* (bad blood) and *Namlueang sia* (bad lymph)

Eight informants mentioned that *luead sia* (bad blood) and *namlueang sia* (bad lymph) resulted in developing *mareng*. The definition of *luead* and *namlueang* in TTM is not clear. *Luead* is recognised as the basic fluid of the body. Therefore, blood is generally accepted as a translation of *luead*. *Namlueang* is recognised as a specific fluid and is referred to as watery secretions. *Luead* and *namlueang* can be in different states, such as normal or bad. Some reports or books might detail their conditions to be spoiled or rotten or poisonous, but we used ‘bad’ (especially for *namlueang*) as a generic term to describe abnormal states since this term needs to be characterised further (in medical-linguistic terms). Interculturally, our findings that bad *luead* and *namlueang* could cause *mareng* corresponds to the description of Brun and Schumacher from Northern Thailand (Brun and Schumacher, 1994) and Maya healers in Guatemala (Berger-González et al., 2016). Similarly, Hausa/Fulani healers in Northern Nigeria stated that cancer of male and female gonads and inflammation are caused by excessive production and deposition of fluids and phlegm (Abubakar et al., 2007).

*Luead* and *namlueang* are also involved with other causes of *mareng* which are the imbalance of the four elements and *fi* (abscesses). According to *Khamphi Maha Chotarat* (a scripture that describes the symptoms and herbal remedies for abnormal menstrual blood and menstruation), rotten or toxic blood could develop to *fi* (Foundation for the Promotion of Thai Traditional Medicine and Ayurved Thamrong School Center of Applied Thai Traditional Medicine, 2007b).

In *mareng* therapy, medicinal plants used to treat *namlueang* problems are important ingredients. *Khaoyennuea* and *khaoyentai*, roots from *Smilax* spp. (see Table 3), are well-known mixtures of botanical drugs used for cancer treatment in Thailand (Itharat et al., 2004). They are used traditionally for *namlueang* problems. Informant C used them to make a decoction for patients with *mareng* in the breast. Extracts from rhizomes of *Smilax glabra* Roxb. (Smilacaceae), which is a major source for *khaoyentai* (Boonyaratanakornkit and Chanthornpteawan, 1993), showed significant growth inhibition to cancer cells of colon, gastric, lung, bladder, breast, liver, prostate, cervix, and human leukaemia cells in *in vitro*, while exhibiting low cytotoxicity to human umbilical vein endothelial cells and normal gastric epithelial cell line GES-1. Mechanistically, this has been linked to cell cycle arrest at S phase, apoptosis induction, and autophagy induction via redox-dependent ERK1/2 pathway (She et al., 2015).

Nowadays, *namlueang* in TTM is often associated with the immune system. Therefore, medicinal plants that are good for *namlueang* might impact positively on the immune system and this can be used as a model to test their pharmacological properties. Water extract from *S. glabra* exhibited immunomodulatory activities by down-regulating over-activated macrophages, up-regulating the dysfunctional T lymphocytes in adjuvant-induced rats (Jiang et al., 2013); and promoting macrophage phagocytosis and increasing macrophage-derived biological factors, including nitric oxide (NO), interleukin-6 (IL-6), tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-1 $\beta$  (IL-1 $\beta$ ) secretion (Wang et al., 2017). *Thaowanpriang* (*Derris scandens* (Roxb.)) contains flavonoids that exhibited specific cytotoxicity against several breast cancer cell lines in *in vitro* and its extract also increased lymphocyte proliferation and NK cells functions (Table 2).

Moreover, informant C stated that abnormal *namlueang* causes inflammation (*kan aksep*) by over-activation of the fire element. Informant A also pointed that the obstruction of blood resulted in an accumulation of waste. These show that bad *luead* and *namlueang* are not only directly involved in *mareng* development, but also facilitate other characteristics.

### 3.3.2 Inflammation (*kan aksep*)

Five informants mentioned that inflammation (*kan aksep*) was related to *mareng* development. Inflammation can be caused by over-activation of the fire element, or external factors, such as food and microorganisms; or constantly impact on an organ. According to informant C, inflammation is a result of an abnormality of *namlueang*. The concept of inflammation and *mareng* is similar to the Ayurvedic concept of cancer, which describes cancer as being of two types; inflammatory and non-inflammatory swellings (Balachandran and Govindarajan, 2005). Thus, this might be due to the influence of Traditional Indian medicine onto TTM (Chokevivat and Chuthaputti, 2005). It is also in agreement with the current knowledge that chronic inflammation is a risk factor in cancer development (Candido and Hagemann, 2013). Inflammation is a defence mechanism of the body to infections and some conditions, such as trauma and toxins. Chronic inflammation is known to be associated with tumourigenesis. It assists cancer cells to acquire hallmarks capabilities, such as sustaining proliferation, limiting cell death, facilitating angiogenesis and metastasis. Nowadays inflammation is accepted as enabling characteristics of cancer (Hanahan and Weinberg, 2011).

### 3.3.3 Chronic illnesses/*krasai*

Every informant said that *mareng* is very difficult to treat. Five informants mentioned specifically that chronic bruises and wounds could develop into *mareng*. According to the informants, chronic conditions can be used to differentiate *mareng* from another disease. For instance, vaginal discharge can result from a problem of the urinary system and dysmenorrhea can result from menstrual blood (*ra-du*) problems. However, informant B suspected *mareng* in the uterus of a patient because this patient had the symptoms for a long time. When a person has a prolonged illness, *krasai* would develop. According to the official Thai dictionary, *krasai* is characterised by emaciation, yellow skin, and cold feet and results in a deterioration of the body (Royal Society of Thailand, 2011). It is also defined as a condition with symptoms generally located in the lower abdominal area, including symptoms recognised in biomedicine as hernia, urino-genital afflictions, ulcers, and possibly gallbladder illness (Bamber, 1987); and a deterioration of the four elements or a decline of the body (Foundation for the Promotion of Thai Traditional Medicine and Ayurved Thamrong School Center of Applied Thai Traditional Medicine, 2007a). Consequently, *krasai* can be described as a degeneration of the body or an organ. As such it is a type of degenerative disease in TTM.

The biomedical relationship between degeneration and cancer is generally linked to mitochondrial dysfunction. Mitochondrial DNA (mtDNA) plays a crucial role in maintaining normal functions of organelles. The accumulation of mtDNA mutations or a decrease in mtDNA copy number have an effect on energy production, cell survival, and increase ROS generation. These have been linked to aging, age-related diseases, and cancer (Hsu et al., 2016b).

### 3.3.4 Accumulation of waste (*khong sia*)

One of the key therapeutic strategies to tackle *mareng* is to remove *khong sia* (waste). *Khong sia* is a very broad term, including body waste, such as urine, excrement, and sweat; as well as accumulated blood clots in the womb and unexcreted food in the intestines. According to *Khamphi Maha Chotarat*, blood clots in the womb are very dangerous since they cause pain and death. To treat the clots, one should take medicines that nourish fire element to re-balance the four elements, followed by a blood tonic (Foundation for the Promotion of Thai Traditional Medicine and Ayurved Thamrong School Center of Applied Thai Traditional Medicine, 2007b). Poonthananiwatkul et al. (2015) reported that medicinal plants used for

detoxification have been taken widely by cancer patients in Thailand and they produced some benefits, such as laxative effect and improved blood test results and breathing in patients (Poonthananiwatkul et al., 2015). Accumulated waste also causes *krasai*, so removal of waste also helps to prevent it.

A Thai medicinal plant that is the best known for its detoxifying properties is *rangchued* (*Thunbergia laurifolia* Lindl.). Its decoction was mentioned by eight informants to be used in *mareng* treatment and prevention. It also has been reported for anti-cancer, anti-inflammatory, and general protective effects (Table 2).

### 3.3.5 Imbalance of *dhātu si* (four basic elements); earth, water, wind, and fire

Three informants mentioned the imbalance of *dhātu si* (the four basic elements) as a cause of *mareng*. The imbalance of the body's basic elements causing *mareng* is also an important explanatory model in Ayurvedic medicine. Cancer is seen as a result of a loss of coordination between three main systems in the body, which are air, fire, and water elements (Balachandran and Govindarajan, 2005). The balance of elements is the main focus of TTM, as well as in other traditional medical systems. It is seen to maintain normal functions of the body and keep one healthy. Every herbal remedy has to contribute to maintaining or re-balancing health.

To link the balance of the elements to pharmacological models, we propose here that such preparations could be involved in homeostasis. Homeostasis is a state of balance within the body or cells. This state maintains normal function and structure of the body or cells. Losing homeostasis plays an important role in carcinogenesis. For example, the production of cell proliferative signals is carefully controlled in normal tissues to ensure a suitable number of cells and to maintain tissue homeostasis. Cancer cells can avoid this regulation and continue to proliferate, grow, and invade nearby tissues and form tumours (Hanahan and Weinberg, 2011).

*Triphala* is a well-known herbal medicine used widely in the treatment and prevention of many diseases. It balances the elements, nourishes blood, and cleans the body. A large body of evidence supports that the medicine is beneficial in cancer and inflammation treatment. It also exhibited immunomodulatory and protective effects (Table 2).

### 3.4 Treatment of *mareng*

The practitioners combine several methods to treat *mareng* patients, such as herbal medicine, or herbal medicines combined with massage, or herbal medicine combined with spiritual methods (such as ritual blessings). For herbal medicines, the practitioners obtained herbal formulation from several sources, including those used by their ancestors in the form of notebooks or verbal; widely used *khamphi* (scriptures), especially *Phaetthayasat Songkhro* and *Tamrayaklangbaan*; or through apprenticeship of famous traditional practitioners.

Prescriptions depend on patients' condition and stages of *mareng*. At the beginning of the treatment, the informants evaluate the suitability of the first therapy in the initial 3-7 days to see the compatibility with the patient's body and good signs for the efficacy. If it does not improve any of the patient's conditions, they will change to the next herbal remedy until they find the right one. The duration of the treatment depends on the disease progress. For instance, an informant recalled a patient with advanced liver cancer (based on a diagnosis from the hospital) who lived up to one year, while in another case with colorectal cancer the person has been on the treatment for four years and still continued the therapy (the interview was performed in April 2013).

Apart from killing *mareng*, there are also other important steps in the treatment. The first one is detoxification as it is believed that accumulated waste in the body may cause *mareng*. Another one is enhancing immunity. Some practitioners also prescribe “*Ya-tat-rak*” (a remedy that kills the ‘root’ of *mareng*) to prevent the recurrence. For example, *ya-tat-rak* from one informant from Lamphun contained *phakwanban* (*Sauropus androgynous*) and *phakdeed* (*Solanum spirale*) (Table 3). As mentioned previously, some TTM practitioners see *mareng* as a living entity and it has roots. Even though the patients have recovered, *mareng* will grow again if they don’t kill the roots.

During and after the treatment, the patients have to avoid some food items which are believed to worsen the condition. Some prohibited food items are catfish, Indo-Pacific mackerel, prawns, shrimps, shellfish, crabs, beef, poultry, sausages, eggs, pineapples, corns, Chinese kale, cucumbers, oyster mushroom (specific to some types of *mareng*), and pickled food. Food restrictions are common knowledge in traditional medicine. Catfish, mackerel, shellfish, shrimps, crabs, chicken, beef, and pickled food are general food prohibitions which are not specific to a disease. Patients just have to avoid them after they started to have health problems. In Northern Thailand, eggs are restricted in some diseases, such as *khaan lidsaduan* (lesions of gums/mouth/nose/eyes/throat/skin), *bahen* (a group of skin diseases), and *saan* (tumours). Traditional practitioners in Northern Thailand also prohibit some food items which are similar to tumours, such as everything with head or round fruits or fingers, grows by root sprouts, also food with sap because it could make tumours become ripe and pus might develop (Brun and Schumacher, 1994).

### 3.5 Medicinal plants used in the treatment/prevention of *mareng*

In general, herbal medicines used in TTM are poly-herbal formulae. Some of herbal combinations used for *mareng* treatment/prevention were highlighted by the informants and described in the case studies. Table 2 presents herbal ingredients mentioned in the case studies with their *in vivo* and/or *in vitro* pharmacological activities related to cancer treatment/prevention. Species recorded as being used but for which there is no confirmed identification are listed in Table 3. This is either because they are introduced/imported or they did not flower during the study period or they were collected in the form of dried herbal materials. Tentative scientific names were suggested for these species by using the relevant literature, information from botanical gardens, especially Siri ruckhachati Nature Learning Park (Mahidol University), Chanthaburi botanical garden (Chanthaburi), and His Majesty the King’s 72<sup>nd</sup> Birthday Anniversary Park—(Faculty of Medicine Siriraj Hospital, Mahidol University).

Traditional uses of each drug are shown in Table 2 and 3. This information was obtained from TTM scriptures or other local sources or from the informants. Out of fifteen drugs, eight are used to treat fever. Four drugs each are used to treat bad *namlueang*, wounds, skin diseases, and poisoning. Three drugs are used to treat *fi* (abscesses) and two are used to treat *krasai*. This helps in the interpretation of the five characteristics of *mareng*. It also helps explaining the actions of each ingredient in a remedy for *mareng* or in its prevention. For example, green mung beans and *T.laurifolia* and *triphala* are used together to prevent *mareng*. Individually, *T.laurifolia* treats fever and poisons and *triphala* balances the four elements. Green mung beans are used to treat over-heating. Since fever/heat is associated with elevated fire element and fire element is linked to development of *mareng*, green mung beans are an emically appropriate and thus important ingredients in *mareng* prevention.

Available scientific evidence suggested pharmacological activities related to cancer treatment/prevention of these herbal ingredients, such as cytotoxicity to cancer cells, anti-



inflammatory activity, and protective effects. Although they were mostly *in vitro* or *in vivo* data, the information is useful for a better understanding of potential actions of these herbal medicines in *mareng* treatment/prevention. For instance, *thaowanpriang* (*D.scandens*) which was mentioned as an ingredient in a *mareng* therapy by informant A is cytotoxic to several breast cancer cells, and exhibited anti-inflammatory, immunomodulatory, and antioxidant effects (Table 2). However, as is generally the case, the evidence is at an *in vivo* or *in vitro* level only.

#### 4. Conclusion

The main objective of this analysis has been to contribute to a dialogue between what constitutes an understanding of illness in traditional medicine, and, more specifically, TTM and the biomedical disease concepts potentially linked to these culturally defined illnesses. Very often there has been a lack of a careful assessment of what the underlying concepts are relating to diseases labelled in English as ‘cancer’. Here we demonstrate that it is possible to understand an indigenous concept, in this case TTM, by using combining medical anthropological approaches and a comparison with biomedical data. For the first time the main characteristics of *mareng* were analysed. Based on the current available evidence, it is not yet possible to draw a conclusion on the theory of *mareng* and on targets for the treatment and prevention of *mareng* in TTM.

Equally, since complex mixtures of herbal remedies are used and since these species are not known very well pharmacologically and clinically, the assessment of their effects will need more detailed studies. Four characteristics - waste accumulation, chronic illnesses/*krasai*, inflammation, and bad *luead* and *namlueang* - are useful in planning more specific assays to investigate bioactivities of herbal medicines. However, a better understanding of the imbalance of the four elements is still needed before combining it to experimental design. The information is relevant not only for the planning of clinical studies or pharmacological experiment in the search for novel compounds for cancer treatment and prevention, but also for the integration of TTM in cancer care.

There were some limitations of this study that need to be highlighted. Firstly, there is no clinical evidence for any of the treatments mentioned, but this is beyond the scope of this study. However, instead it demonstrates plausible mechanisms which can be investigated further. Secondly, even though the number of participants (33) is sufficiently large to understand the basic concepts, it is too small to conclude that the results represented an overall perspective of TTM practitioners’ knowledge. However, we interviewed informants from different parts of the country to make sure the overall views, as well as influences of local culture, herbal medicine resources, and the indigenous medical knowledge on the healing practice are covered. Thirdly, there was no clinical evidence to confirm practitioners’ diagnosis of *mareng*. The informants knew that their patients have cancer because they informed them so. Plants are generally sourced locally. Therefore, there may be a chemical variability of the starting material and there are likely to be differences in the composition of the preparations based on extraction methods and different value chains. However, in general, these chains are relatively short with the healer in control of the entire chain (Booker et al., 2012). Lastly, we did not observe any real diagnosis or consultation or treatment intervention as these were not included in the ethical approval.

For future studies, a larger number of informants should be included to ascertain the findings. Observational studies combining TTM and biomedical diagnosis of a patient, and clinical studies combining the TTM treatments and conventional cancer therapy would be an ideal next step. This could follow the model of reverse pharmacology. It has to be part of a strategy

to better understand treatment outcomes for a set of diseases which is both devastating and of great importance both in TTM and in biomedicine. Specifically, *mareng* is a very complex condition and need to be understood in much more involving collaborations between TTM practitioners and biomedical doctors/researchers.

#### **Conflict of interest statement**

The authors declare no conflict of interest.

#### **Authors contributions**

NL performed the fieldwork, analysed the data, and wrote the manuscript.

JT performed the fieldwork and wrote the manuscript.

SB collected the plants and prepared the voucher specimens.

RB performed the fieldwork and prepared the voucher specimens.

PA and TL participated in the data interpretation.

MH performed the fieldwork, analysed the data, and wrote the manuscript.

All authors read and approved the final manuscript.

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**Table 2** List of plants/ingredients mentioned in the case studies, their traditional uses, and published relevant pharmacological properties

Local names	Part used	Scientific names	Voucher number	Traditional uses	Relevant pharmacological properties
Thaowanpriang	stems	<i>Derris scandens</i> (Roxb.) Benth. (Fabaceae)	PBM05189	To fix <i>en</i> (tendon or ligament) problems, treatment of cough, cold, and <i>krasai</i> , diuretic (I, T, K, M, A)	<p>Cytotoxicity to cancer cells</p> <ul style="list-style-type: none"> <li>- Methanol extract/flavonols exhibited cytotoxic activity against MDA-MB-231 and MCF-7 breast cancer cells and Topoisomerase II poison activity in yeast cells (Ausawasamrit et al., 2015; Sangmalee et al., 2016; Tedasen et al., 2016).</li> </ul> <p>Anti-inflammatory activity</p> <ul style="list-style-type: none"> <li>- <i>In vitro</i>, water extract/ethanol extract/genistein inhibited inflammatory substances; including myeloperoxide and eicosanoids (Laupattarakasem et al., 2004; Laupattarakasem et al., 2003)</li> <li>- In the rat hind paw oedema test, the water extract reduced the oedema when given intraperitoneally, but not when given orally (Laupattarakasem et al., 2003).</li> </ul> <p>Immunomodulatory activity</p> <ul style="list-style-type: none"> <li>- The ethanol extract enhanced lymphocyte proliferation and NK cell activity of normal individuals and induced NK cell activity of HIV-infected participants. It also increased IL-2 secretion from normal PBMC, but not IL-4 (Sriwanthana and Chavalittumrong, 2001).</li> </ul> <p>Anti-oxidant activities</p> <ul style="list-style-type: none"> <li>- Its hexane and chloroform extracts showed moderate free radical scavenging activities (Rao et al., 2007).</li> </ul>
Khanunsampalo, sake (breadfruit)	roots	<i>Artocarpus altilis</i> (Parkinson ex F.A.Zorn) (Moraceae)	PBM05203	Treatment of sexually transmitted diseases and <i>mareng</i> (I)	<p>Cytotoxic and anti-tumour activities</p> <ul style="list-style-type: none"> <li>- Diethyl ether extract/methanol extracts/partially purified fraction/geranyl dihydrochalcone showed cytotoxicity in T47D breast cancer and DU145 prostate cancer cells and suppressed tumour growth in DU145 xenograft initiation model (Arung et al., 2009; Jeon et al., 2015).</li> </ul> <p>Protective effects</p> <ul style="list-style-type: none"> <li>- The water and ethanol extracts reduced serum AST, ALT and ALP levels in CCl<sub>4</sub>-treated rats and restored total protein and albumin to near normal levels. It also</li> </ul>

Local names	Part used	Scientific names	Voucher number	Traditional uses	Relevant pharmacological properties
					<p>suppressed TBARS and increased glutathione level (Sairam et al., 2016).</p> <p>Activities related to blood and lymph</p> <ul style="list-style-type: none"> <li>- Intravenous administration of the water extract of the leaves caused significant hypotensive and bradycardia responses (Nwokocha et al., 2012).</li> <li>- Ethanol extract of the leaves showed a potent ACE-inhibitory activity with an IC<sub>50</sub> value of 54.08 ± 0.29 µg/mL (Siddesha et al., 2011).</li> </ul>
Makhampom	roots, fruits	<i>Phyllanthus emblica</i> L. (Phyllanthaceae)	PBM05199	<p>Young fruit: nourish muscle and voice</p> <p>Mature fruit: treatment of fever (S, M)</p>	<p>Cytotoxicity to cancer cells</p> <ul style="list-style-type: none"> <li>- Water extract/geraniin/isocorilagin showed cytotoxicity against MCF-7 cells, HELF cells, and HT1080 and down-regulated MMP2 and MMP9 gene expressions in human fibrosarcoma cells HT1080 (Liu et al., 2012; Yahayo et al., 2013)</li> </ul> <p>Anti-inflammatory activity</p> <ul style="list-style-type: none"> <li>- Ethanol extract of the branch suppressed the expression of LPS-induced pro-inflammatory genes (COX-2, iNOS, TNF-alpha, IL-16 and IL-6) in RAW 264.7 and also suppressed the carrageenan-induced paw oedema in rats (Sripanidkulchai and Junlatat, 2014).</li> </ul> <p>Protective effects</p> <ul style="list-style-type: none"> <li>- Administration of the fruits/methanol extract of the leaves/ compounds isolated from the fruits showed protective effects against cognitive deficits, biochemical abnormalities, apoptosis induced by aluminum chloride, and tau hyperphosphorylation (Thenmozhi et al., 2016), cadmium-induced neurotoxicity in mice (Chatterjee et al., 2016), CCl<sub>4</sub>-induced oxidative injuries and tissue damage of lungs of rats (Tahir et al., 2016), H<sub>2</sub>O<sub>2</sub>-induced injury in PC12 cells (Zhang et al., 2016), and chemical-induced liver injuries in several animal models (Variya et al., 2016).</li> </ul> <p>Immunomodulatory activity</p> <ul style="list-style-type: none"> <li>- The fruit extract reversed the immunosuppressive effect of Cr (VI), enhanced white blood cell count and % lymphocyte distribution in mice, and also activated macrophages (Belapurkar et al., 2014) and the isolated compounds, geraniin and isocorilagin, stimulated splenocyte proliferation (Liu et al., 2012).</li> </ul> <p>Activities related to blood and lymph</p>

Local names	Part used	Scientific names	Voucher number	Traditional uses	Relevant pharmacological properties
					<ul style="list-style-type: none"> <li>- Water extract decreased haemolytic activity in red blood cells of human subjects receiving chronic alcohol and cigarette smoking (Lokesh et al., 2016).</li> </ul>
Thuakheaw (green mung beans)	dried seeds	<i>Vigna radiata</i> (L.) R. Wilczek (Fabaceae)	-	Diuretic, tonic, treatment of over-heat, nourish joints (I, K)	<p>Anti-inflammatory activity</p> <ul style="list-style-type: none"> <li>- <i>In vivo</i>, water extract/ethanol extract showed potent anti-inflammatory and antinociceptive activities (Ali et al., 2014; Venkateshwarlu et al., 2016).</li> <li>- <i>In vitro</i>, water extract/methanol extract/ethanol extract inhibited NO, COX-2, and exhibited membrane stabilization activity and protein denaturation activity (Ali et al., 2014; Venkateshwarlu et al., 2016; Zia-Ul-Haq et al., 2013).</li> </ul> <p>Immunomodulatory activity</p> <ul style="list-style-type: none"> <li>- Polysaccharides from the seeds enhanced the production of NO, TNF-<math>\alpha</math>, and IL-6 in RAW 264.7 cells (Yao et al., 2016).</li> </ul> <p>Protective effects</p> <ul style="list-style-type: none"> <li>- <i>C. militaris</i>-fermented mung beans protected DNA damage (Xiao et al., 2015).</li> <li>- Mung bean coat extracts attenuated LPS-induced release of HMGB1 and several chemokines in macrophage cultures. It also rescued mice from lethal sepsis (Zhu et al., 2012).</li> </ul>
Rangchued	leaves	<i>Thunbergia laurifolia</i> Lindl. (Acanthaceae)	PBM05178	Universal antidote, treatment of fever, thirst (T, M)	<p>Protective effects</p> <ul style="list-style-type: none"> <li>- <i>In vitro</i>, water extract/ethanol extract/acetone extract showed protective effects against oxidative stress in HepG2 cells (Rocejanasaroj et al., 2014), increased QR activity in Hepa1C1C7 cells and showed antimutagenic activity in <i>Salmonella typhimurium</i> TA 98 (Oonsivilai et al., 2007), ethanol-induced cell death of primary rat hepatocytes (Pramyothin et al., 2005).</li> <li>- <i>In vivo</i>, leaves/water extract/ethanol extract showed protective effects against cadmium toxicity in rats (Ruangyuttikarn et al., 2013), inflammation-induced by <i>O. viverrini</i> infection or with NDMA administration (Wonkchalee et al., 2012), and ethanol-induced liver injury (Pramyothin et al., 2005). It also protected <i>Oreochromis niloticus</i> from Pb(NO<sub>3</sub>)<sub>2</sub> toxicity (Palipoch et al., 2011).</li> </ul> <p>Anti-inflammatory activity</p> <ul style="list-style-type: none"> <li>- Rosmarinic acid isolated from the leaves exhibited antinociceptive activity in the hot-plate test, reduced acetic acid-induced writhing, suppressed formalin-induced pain in the early and late phases, reduced carrageenan-induced and PGE<sub>2</sub>-induced</li> </ul>

Local names	Part used	Scientific names	Voucher number	Traditional uses	Relevant pharmacological properties
					<p>paw oedema, and inhibited cotton pellet-induced granuloma formation in mice (Boonyarikpunchai et al., 2014).</p> <ul style="list-style-type: none"> <li>- The powder showed anti-inflammatory properties in <i>O. viverrini</i> and NDMA-treated Syrian hamsters by reducing the aggregation of inflammatory cells surrounding the hepatic bile ducts and reversed serum ALT, ALP, BUN and creatinine levels to normal (Wonkchalee et al., 2012).</li> </ul>
Triphala	fruits	A mixture of the fruits from <i>Phyllanthus emblica</i> L. (Phyllanthaceae), <i>Terminalia bellirica</i> (Gaertn.) Roxb. (Combretaceae), <i>Terminalia chebula</i> Retz. (Combretaceae)	-	Balance the elements, tonic, nourish water element so this improves blood circulation, improve digestive system, cleansing especially waste in the intestine (I, S)	<p>Cytotoxicity to cancer cells</p> <ul style="list-style-type: none"> <li>- Methanol extract/chebulinic inhibited proliferation and induced apoptosis in human colon cancer stem cells (Vadde et al., 2015) and suppressed VEGF- induced angiogenesis (Lu et al., 2012).</li> </ul> <p>Anti-inflammatory activity</p> <ul style="list-style-type: none"> <li>- A randomized controlled clinical trial with 90 volunteers with chronic gingivitis showed that the effectiveness of Triphala mouthwash in the treatment of gingivitis was comparable to that of chlorhexidine mouthwash (Pradeep et al., 2016).</li> <li>- Water extract inhibited LPS-induced inflammatory responses in RAW 264.7 cells and adjuvant-induced arthritic rats by inhibition of NF-κB pathway (Kalaiselvan and Rasool, 2016).</li> <li>- Triphala recipe (4 mg/ear) showed an inhibitory effect on the ear oedema formation in rats induced by ethyl phenylpropiolate, but not by arachidonic acid. Furthermore, It also decreased carrageenan-induced hind paw oedema and showed antinociceptive effect in formalin-treated mice (Sireeratawong et al., 2013).</li> </ul> <p>Immunomodulatory effects</p> <ul style="list-style-type: none"> <li>- Administration of Triphala showed immunomodulatory effects on neutrophil functions, IL-2, IFN-γ levels, CD4+/CD8+lymphocyte phenotype, mitogen-induced T-lymphocyte proliferation, as well as increased phagocytic functions in mice (Belapurkar et al., 2014).</li> <li>- In a clinical trial phase I, volunteers who administered Triphala 3 capsules/ day for 2 weeks showed increase activity of cytotoxic T cells (CD3<sup>+</sup>CD8<sup>+</sup>) and natural killer cells (CD16<sup>+</sup>CD56<sup>+</sup>) compared to control group (Phetkate et al., 2012).</li> </ul> <p>Protective effects</p> <ul style="list-style-type: none"> <li>- Water extract/ethanol extract exhibited protective effects against X-radiation and bleomycin-induced DNA breaks and suppressed ROS generation in HeLa cells</li> </ul>

Local names	Part used	Scientific names	Voucher number	Traditional uses	Relevant pharmacological properties
					(Takauji et al., 2016), H <sub>2</sub> O <sub>2</sub> -induced damage in fibroblasts or HaCaT cells, and decreased the mRNA levels of tyrosinase in B16F10 cells (Varma et al., 2016).
Yamornoi, Yadokkhao	whole plants, leaves	<i>Cyanthilium cinereum</i> (L.) H. Rob (Asteraceae) (synonym: <i>Vernonia cinerea</i> (L.) Less.)	PBM05200	Relief of stomachache, fever, cough, jaundice, haemorrhoid, pus, eye problems, healing wounds, anti-flatulent, tonic, and cleansing the lung (I, M, B)	<p>Cytotoxic and anti-tumour activities</p> <ul style="list-style-type: none"> <li>- <i>In vitro</i>, dichloromethane fraction of the ethanol extract/ vernolide-A exhibited anti-cancer activity against HeLa, A549, MCF-7, Caco-2 (Beeran et al., 2014) and B16F-10 melanoma cells (Pratheeshkumar and Kuttan, 2011d, e).</li> <li>- <i>In vivo</i>, methanol extract/veranolide-A reduced lung tumour formation, metastasis, elevated level of serum IL-1<math>\beta</math>, IL-6, TNF-<math>\alpha</math>, and GM-CSF, and VEGF induced by angiogenesis, and increased life span of C57BL/6 mice (Pratheeshkumar and Kuttan, 2011c, e).</li> </ul> <p>Anti-inflammatory activity</p> <ul style="list-style-type: none"> <li>- <i>In vitro</i>, sesquiterpene lactones isolated from hexane extract of the flower suppressed TNF-<math>\alpha</math>-induced NF-<math>\kappa</math>B activity and NO production in LPS-stimulated RAW 264.7 cells (Youn et al., 2012).</li> <li>- <i>In vivo</i>, intraperitoneal administration of methanol extract inhibited the PMA-induced superoxide generation in mice peritoneal macrophages, increased the levels of catalase, superoxide dismutase, glutathione, glutathione peroxidase and glutathione-S transferase in blood and liver, decreased lipid peroxidation, and inhibited carrageenan-induced inflammation in BALB/c mice (Kumar et al., 2009).</li> </ul> <p>Immunomodulatory activity</p> <ul style="list-style-type: none"> <li>- Methanol extract and vernolide-A stimulated cytotoxic T lymphocyte, NK cell, antibody-dependent cellular cytotoxicity, and antibody-dependent complement-mediated cytotoxicity through enhanced secretion of IL-2 and IFN-<math>\gamma</math> in <i>in vivo</i> and <i>in vitro</i> (Pratheeshkumar and Kuttan, 2012).</li> <li>- Vernolide-A increased the production of IL-2 and IFN-<math>\gamma</math> in metastatic tumour-bearing mice. It downregulated the serum levels of IL-1<math>\beta</math>, IL-6, TNF-<math>\alpha</math>, and granulocyte-macrophage colony-stimulating factor (GM-CSF) during metastasis in C57BL/6 mice (Pratheeshkumar and Kuttan, 2011a).</li> </ul> <p>Protective effects</p> <ul style="list-style-type: none"> <li>- Intraperitoneal administration of the methanol extract exhibited protective effects against gamma radiation-induced immunosuppression and oxidative stress in</li> </ul>

Local names	Part used	Scientific names	Voucher number	Traditional uses	Relevant pharmacological properties
					BALB/c mice, while it did not compromise the effectiveness of the radiotherapy (Pratheeshkumar and Kuttan, 2011b).
Phlukhao, Phakphaotong	whole plants	<i>Houttuynia cordata</i> Thunb. (Saururaceae)	PBM05204	Treatment of sexually transmitted diseases, bad <i>namlueang</i> , wounds, fever, heat, lung problems, oedema, cough, haemorrhoids, diuretic, use externally for snake and insect bites, skin diseases, abscess, <i>mareng khuttharat</i> (P, M)	<p>Cytotoxicity to cancer cells</p> <ul style="list-style-type: none"> <li>- Its extracts/fractions exhibited cytotoxicity against nasopharyngeal carcinoma cells (Chen et al., 2016), lung cancer A549 cells (Chen et al., 2013), and human leukemic Molt-4 cells (Pommaban et al., 2012).</li> <li>- Fermentation products suppressed the growth of HeLa, HCT116, HT29 cells, human leukemic HL-60 and Molt-4 cell, and HepG2 cells (Banjerdpongchai and Kongtawelert, 2011; Senawong et al., 2014).</li> </ul> <p>Anti-inflammatory activity</p> <ul style="list-style-type: none"> <li>- Ethanol extract from the poultice exhibited anti-bacterial effects and anti-biofilm against methicillin-resistant <i>Staphylococcus aureus</i> (MRSA), inhibition effect of <i>S. aureus</i> lipoteichoic acid (LTA)-induced IL-8 and CCL20 production in human keratinocyte without any cytotoxicity (Sekita et al., 2016).</li> <li>- Volatile compounds/polysaccharides/flavonoids exhibited anti-inflammatory effects in <i>in vivo</i> (Chen et al., 2014; Lee et al., 2015; Li et al., 2013; Park et al., 2013; Xu et al., 2015).</li> <li>- Ethanol extract/ethyl acetate fraction/volatile oil suppressed the production of inflammatory markers/ cytokines in LPS-stimulated RAW 264.7, LPS-stimulated mouse peritoneal macrophages, and HMC-1 human mast cells (Chun et al., 2014; Lee et al., 2013; Li et al., 2013; Li et al., 2011).</li> <li>- Hexane extract inhibited prostaglandin synthase in <i>in vitro</i> (Bauer et al., 1996).</li> </ul> <p>Immunomodulatory activity</p> <ul style="list-style-type: none"> <li>- Water extract/ethanol extract/polysaccharides possessed immunomodulatory effects on the vaginal mucosa (Sathakarn et al., 2015), PBMCs (Cheng et al., 2014), LPS-activated macrophages (Kim et al., 2009), mouse splenic lymphocytes (Lau et al., 2008), Jurkat T cells and HMC-1 human mast cell line (Lee et al., 2008), mast cell-mediated anaphylactic responses (Li et al., 2005).</li> </ul> <p>Protective effects</p> <ul style="list-style-type: none"> <li>- Ethyl acetate extract exhibited hepatoprotective effect in CCl<sub>4</sub>-induced hepatotoxicity in mice (Kang and Koppula, 2014)</li> <li>- Water extract showed protective effect against high saturated fat diet-induced</li> </ul>



Local names	Part used	Scientific names	Voucher number	Traditional uses	Relevant pharmacological properties
					obesity and oxidative and inflammatory injury in mice (Lin et al., 2013), prevent lung injury from LPS stimulation in rats (Cai et al., 2013), cardiac and renal injury and oxidative stress under diabetic condition in mice (Hsu et al., 2016a), and ethanol extract also reduced atherogenic risk and hepatic oxidative damage induced by high saturated fat diet in rats (Kim et al., 2014).
Kasalong, Peeb (Indian cork tree)	roots, stem barks	<i>Millingtonia hortensis</i> L.f. (Bignoniaceae)	PBM05202	Nourishment of lung, treatment of tuberculosis and lung problems (P, M)	<p>Cytotoxicity to cancer cells</p> <ul style="list-style-type: none"> <li>- Water extract and its fraction inhibited cell proliferation and induced apoptosis in RKO colon cancer cells (Tansuwanwong et al., 2009).</li> </ul> <p>Antimutagenic activity</p> <ul style="list-style-type: none"> <li>- Hispidulin and hortensin showed antimutagenic activity against 2-aminoanthracene, aflatoxin B1, and dimethylnitrosamine, while showed no mutagenicity and no cytotoxicity toward <i>S. typhimurium</i> strains TA98 and TA100 (Chulasiri et al., 1992).</li> </ul> <p>Anti-inflammatory activity</p> <ul style="list-style-type: none"> <li>- Hispidulin inhibited 5-LOX in <i>in vitro</i> (Moongkarndi et al., 1991).</li> </ul>
Yapakkhwai	Whole plant	<i>Dactyloctenium aegyptium</i> (L.) Willd. (Poaceae)	PBM05201	Nourishment of fire element; treatment of fever; use externally for treatment of swelling, aching, and inflammation (M)	N/A

I = uses mentioned by informant (s)

S = Khamphi Sappakhunya (Foundation for the Promotion of Thai Traditional Medicine and Ayurved Thamrong School Center of Applied Thai Traditional Medicine, 2007c)

T = Thaicrodedrug.com by Faculty of Pharmaceutical Sciences, Ubon Ratchathani University (Homhual, 2010b)

P = Phargarden.com by Faculty of Pharmaceutical Sciences, Ubon Ratchathani University (Homhual, 2010a)

K = Khamphi Krasai (Foundation for the Promotion of Thai Traditional Medicine and Ayurved Thamrong School Center of Applied Thai Traditional Medicine, 2007a)

M = Mai Thet Meung Thai (Pongboonrod, 1979)

A = (Osiri et al., 2011)

B = (Picheansoonthon et al., 2001)

**Table 3** List of unresolved plants mentioned in the case studies, suggested species, and their traditional uses

Local names	Part used	Tentative identification	Collection number	Traditional uses
Khokhlan	stems	<i>Mallotus repandus</i> (Willd.) Müll. Arg. (Euphorbiaceae)	NL-0121	To fix <i>en</i> problems, treatment of <i>krasai</i> , renal impairment, diuretic, blood tonic, treatment of internal poisons (I, T)
Khaoyennuea	roots	<i>Smilax corbularia</i> Kunth. (Smilacaceae) or mix <i>Smilax</i> spp. (Boonyaratanakornkit and Chanthornpteptawan, 1993)	NL-0022	Treatment of <i>pradong</i> (fever and itching rash), <i>mareng khuttharat</i> , <i>namlueang</i> problems, <i>en</i> problems, sexually transmitted diseases, thirst, abscesses, ulcers, urination problems, inflammation, eye problems, kill pus, inhibition of poisons in bones. They are normally used together. (S, T, M)
Khaoyentai	roots	<i>Smilax glabra</i> Roxb. (Smilacaceae) or mix <i>Smilax</i> spp. (Boonyaratanakornkit and Chanthornpteptawan, 1993)	NL-0023	
Khanthongphayabat	roots or stem barks	<i>Suregada multiflora</i> (A.Juss.) Baill. (Euphorbiaceae)	NL-0124	Treatment of fever, poisoned blood, lung diseases, worms, <i>namlueang</i> problems, <i>mareng khuttharat</i> , liver diseases, lung diseases, skin diseases, sexually transmitted diseases, and <i>pradong</i> (A, P, M)
Horathaosunak	dried stems	<i>Balanophora abbreviata</i> Blume (Balanophoraceae)	NL-0125	Treatment of asthma, skin diseases, leprosy, and <i>mareng khuttharat</i> (I, M)
Huayang	roots	<i>Smilax ovalifolia</i> Roxb. ex D.Don (Smilacaceae)	NL-0073	Inhibition of poisons in bones and <i>en</i> (M)
Nontaiyak	roots	<i>Stemona tuberosa</i> Lour. (Stemonaceae)	NL-0076	Treatment of skin diseases, itching, bad <i>namlueang</i> , cough, phlegm, piles, <i>mareng</i> in liver, kill worms, use externally for skin diseases, kill scabies and louse (P, M)
Oidam (sugar cane)	stems	<i>Saccharum officinarum</i> L. (Poaceae)	NL-0047	Treatment of asthma, gallstones, cough, thirst, fever, wounds, diuretic, and nourish water element (S, M)
Phakwanban	leaves	<i>Sauropus androgynus</i> (L.) Mer. (Phyllanthaceae)	NL-0046	Inhibition of over-heat, recurrent fever in patients who eat prohibited food (M)
Phakdeed, Dangdeed	roots, seeds	<i>Solanum spirale</i> Roxb. (Solanaceae)	NL-0058	Treatment of chronic wound with pus (M)

I = uses mentioned by informant(s)

S = Khamphi Sapphakhunya (Foundation for the Promotion of Thai Traditional Medicine and Ayurved Thamrong School Center of Applied Thai Traditional Medicine, 2007c)

T = Thaicrudedrug.com by Faculty of Pharmaceutical Sciences, Ubon Ratchathani University (Homhual, 2010b)

P = Phargarden.com by Faculty of Pharmaceutical Sciences, Ubon Ratchathani University (Homhual, 2010a)

M = Mai Thet Meung Thai (Pongboonrod, 1979)

A = (Osiri et al., 2011)

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