

HERB-DRUG INTERACTION DIGITAL PLATFORM FOR CANCER HEALTHCARE

Watchara Kanjanakawinkul¹ Kamon Chaityasit^{2,3} Maethaphan Kitporntheranunt⁴
Watcharachai Wiriyasuttiwong⁵ Latiporn Udomsuk⁶ Sorawuth Pongrojphao⁴

¹Chulabhorn Royal Pharmaceutical Facilities, Chulabhorn Royal Academy, Thailand.

²Integrative Nutrition and Herbal Medicine Association, Pathumthani, Thailand.

³Vitalife Scientific Center, Bumrungrad International Hospital, Bangkok, Thailand.

⁴Faculty of Medicine, Srinakharinwirot University, Nakhon Nayok, Thailand.

⁵Faculty of Engineering, Srinakharinwirot University, Nakhon Nayok, Thailand.

⁶College of Medicine and Public Health, Ubon Ratchathani University, Ubon Ratchathani, Thailand.

ABSTRACT

This research paper presents herb-drug interaction digital platform for cancer healthcare. The objective is to serve as a knowledge hub, database, healthcare assistance tool, and a vital and beneficial community for knowledge exchange among healthcare professionals, patients, and the general public. In this research, the database on herb-drug interaction comprises drug name, pharmacological group, herb name, active ingredient/pharmacological properties, effects, mechanism of interaction, severity, documentation, management, patient-friendly explanation, warning categories, and references. This platform will help address the issue of using herbal remedies in conjunction with current pharmaceutical treatments, which can potentially pose risks to users, especially when interactions between drugs and herbs may occur gradually and go unnoticed until patients experience harm or severe adverse effects on their health. From the digital platform testing conducted in this research using automated testing with Selenium IDE and various test cases, it was found that the system operates correctly in accordance with the designed functions in all aspects.

Keyword: Healthcare Platform, Herb-Drug Interaction, Cancer, Healthcare Application

1. INTRODUCTION

Thailand is a country with a long history of using herbal medicine for the treatment of diseases and illnesses. At present, it is common to find the use of herbal remedies and dietary supplements that include various types of herbs alongside conventional medication for disease treatment.

The concurrent use of herbal remedies and conventional medication as mentioned can potentially lead to herb-drug interactions, which may result in suboptimal outcomes in the treatment with the conventional medication. The interactions between drugs and herbs can be divided into two categories: 1) Pharmacokinetic interactions: These involve how herbs can affect the absorption, distribution, metabolism, and elimination of drugs. 2) Pharmacodynamic interactions: These interactions relate to how herbs can alter the effects, potency, or activity of drugs. They may either reduce a drug's effectiveness to the point where it cannot effectively treat a disease or enhance a drug's effects to the extent that it causes toxicity. From reports in various countries, it has been found that several herbs have clear interactions with conventional drugs. For example: 1) Ginseng (*Panax ginseng* C.A. Meyer) can increase the side effects of imatinib, a tyrosine protein kinase inhibitor used in cancer treatment. This can lead to greater liver toxicity in cancer patients receiving imatinib. 2) Ginkgo (*Ginkgo biloba* Linn.) can increase the risk of bleeding in patients taking aspirin or warfarin, as it contains ginkgo B, which inhibits platelet aggregation. This can result in easier bruising and slower blood clotting. 3) Licorice (*Glycyrrhiza glabra* Linn.) can exacerbate the side effects of prednisolone, an anti-inflammatory medication. When taken together, it can lead to severe side effects such as gastric ulcers or osteoporosis. These interactions highlight the importance of being cautious when combining herbal remedies with conventional medications and consulting with healthcare professionals to avoid potential risks.

From the compilation of data from the Department of Thai Traditional and Alternative Medicine, Ministry of Public Health, it is found that Thailand has a total of 31 databases related to Thai herbal remedies. These databases include: MedThai, Thaicrudedrug.com, Phargarden.com, MED HERB GURU, PHTIC-PERDO KuiHerb Hortdo:

Manuscript received on November 22, 2024; revised on May 1, 2025, accepted on May 8, 2025.

*Corresponding author E-mail: watch@g.swu.ac.th, Department of Computer Engineering, Faculty of Engineering, Srinakharinwirot University, Thailand.

Knowledge Plant Diversity HDC TTM Service, and so on. The analysis of all the databases revealed that the data and data storage systems of each database differ from one another. As a result, if medical professionals or healthcare personnel need to search for information on a particular type of herb, they may have to use at least 2-3 different databases to obtain comprehensive information about that specific herb. This can lead to complexity and delays in accessing the required information, making the process cumbersome. Furthermore, upon surveying the digital healthcare landscape in Thailand, it was identified that the country lacks sources of knowledge, databases, health management tools, knowledge exchange systems, and online health communities specifically focused on the interaction between herbal remedies and pharmaceuticals for cancer patients. This gap in resources affects the healthcare management for cancer patients. Therefore, this research proposes the design and development of a herb-drug interaction digital platform for cancer healthcare. This platform aims to serve as a convenient tool for accessing knowledge, intended for medical professionals and caregivers responsible for cancer patients, as well as the cancer patients themselves. Moreover, it serves as a tool to facilitate accessibility to comprehensive and accurate knowledge about the proper healthcare management through the interaction between herbal remedies and pharmaceuticals. This platform aims to contribute to the well-being of both healthcare professionals and the general public, enabling them to maintain good health and self-care systematically, universally, and at all times.

2. ANTICANCER DRUG-HERB INTERACTION

Cancer is a group of diseases involving abnormal cell growth that grows uncontrollably and spreads to other parts of the body. It can transform nearby healthy cells into cancer cells. The proliferation of abnormal cells causes the body's organs to not function normally, which could lead to death. Cancer is a leading cause of death worldwide, and it will continue to increase. According to Thai public health statistics for 2016–2017, cancer is one of the most common causes of death and has the highest mortality rate (per 100,000 people) in Thailand. The National Cancer Institute in 2021 indicated that liver cancer, cholangiocarcinoma, colon cancer, and lung cancer are more likely to develop in men. Breast, cervical, and colon cancers are the most prevalent cancers in women.

There are various cancer treatments available presently, such as surgeries, radiotherapy, and chemotherapy and immunotherapy drug, etc. which is

the most common method used to treat cancer. In addition, there are also herbs used to treat cancer because some *in vitro* studies suggest that they can prevent cell growth and multiplication, though there is no clear evidence for this as well. However, herbs can reduce the side effects of chemotherapy [1], such as ginger, which can reduce nausea and vomiting. In addition, herbs are supplemented for cancer patients. But even so, improper herb use can result in interactions between cancer drugs and herbs. Interactions can be of two types: [2]

1) Pharmacodynamic interactions

When a drug binds to a receptor, the pharmacodynamic profile (potency and efficacy) of the drug is changed, and the pharmacological effects are also altered.

2) Pharmacokinetic interactions

Pharmacokinetic interactions are "what the body does to the drug." These interactions occur when one drug (the perpetrator) alters the concentration of another drug (the object), with clinical consequences. It can change the concentration of drugs. There are four processes in pharmacokinetics:

a. Absorption - This is the phase in which the drug enters the bloodstream, commonly through the mucous surface. Changes in the physiology or biochemistry of the mucous surface can affect the rate of adsorption and bioavailability, and the speed at which this happens depends on the method of administration.

b. Distribution - The drug is distributed throughout the body after it has entered the bloodstream, moving from the blood into various tissues and organs until it eventually reaches the target site.

c. Metabolism - This phase encapsulates how the drug leaves the bloodstream by metabolism, where the molecular structure of the drug is broken down by mechanisms in the body that use enzymes to increase drug solubility and excretion, where the drug is filtered out. The main organ for metabolism is the liver. The metabolism process has two phases, followed by enzyme groups:

c1) Phase I reactions: This phase consists of oxidation, reduction, hydrolysis, and hydroxylation. Cytochrome P450 (CYP) is used in these processes [3]. In humans, there are 18 families and 44 subfamilies of CYPs. CYP1, CYP2, and CYP3 (such as CYP1A2, CYP2C9, CYP2D6, and CYP3A4) have the function of metabolizing xenobiotics.

c2) Phase II reactions: This process increases solubility by conjugation with substances such as glutathione and glucuronide.

Elimination - The main process of eliminating metabolized drug compounds from the body occurs in urine and feces. Other excretion methods include the lungs or sweating through the skin. Molecular size and charge influence the excretion pathway.

Cancer medication is one of the most important cancer treatments currently available. There are three different types of cancer drugs [4]. The first class of cancer medications to be developed was chemotherapy. This drug contains chemicals that are toxic to all cells, including normal and cancer cells. They have been used for a long time and have well-defined side effects. Even though they are safer and can be used to treat a variety of cancers, they have a lot of side effects. Examples of medicines used in chemotherapy are doxorubicin and etoposide. Second, hormonal treatment is the targeted therapy that has the fewest side effects. Some hormone-related cancers, such as hormone receptor-positive breast cancer, can be treated with hormonal treatment. Tamoxifen is an example of a drug used in hormonal treatment. Third, targeted therapy It's specific to the mechanisms of each cancer pathology, which can increase effectiveness and reduce side effects. Targeted therapy can only affect cancer cells; it has no effect on normal cells. Examples of medicines used in targeted therapy are imatinib and nilotinib.

This article summarizes the enzymes and metabolites that occur in each metabolism process of each cancer drug and offers recommendations on how to use herbs safely in cancer patients because there are numerous cancer drugs available today, each with a variety of mechanisms of action and excretion methods.

Interactions are pharmacological actions that occur between two substances that can change the concentration of the drug in the body, involve inhibition, synergy, increasing or decreasing side effects, toxicity, or have a new activity [5]. There are reports of drug-herb interactions, which indicate that the most common mechanisms of interaction are inhibition and induction of cytochrome P450 [6]. As well as 92.8% of Thailand, approximately 1-2 different types of herbs or herbal supplements are used by one person [7]. There is a prevalence report of about 78% of cancer patients receiving chemotherapy, and there is a risk of occurring drug-herb interactions of 27% [8]. There are various herbs that contain phytochemicals that can inhibit or induce metabolic enzymes, especially CYPs, as was previously mentioned. In addition, CYP substrates are used in the metabolism of many cancer drugs. Consequently,

there is a risk associated with combining cancer drugs and herbs.

Herbs have been reported to inhibit CYP3A4 (CYP3A4 inhibitors). Table 1 shows which herbs can inhibit CYP3A4. Mechanisms of herb-cancer drug interaction that can either increase or decrease cancer drug activity are shown in Table 3. Therefore, it is important to consider and avoid using combinations between herbs and cancer drugs that use CYP3A4 in the metabolism process. If it is necessary to use a combination, closely monitor any side effects.

Herbs have been reported to induce CYP3A4 (CYP3A4 inducers). Table 1 shows which herbs can induce CYP3A4, such as Dong Quai (*Angelica sinensis*). There is a report that ethanal extract from Dong Quai can induce CYP3A4 in HepG2 cells, which can increase the concentration of rifampin that is metabolized via CYP3A4 and raise the concentration up to $118 \pm 2.26\%$ [9]. As a result, it is important to consider and avoid using combinations between Dong Quai and cancer drugs that use CYP3A4 in the metabolism. If it is necessary to use a combination, closely monitor any side effects.

Herbs have been reported to inhibit CYP2C8 (CYP2C8 inhibitors). Table 1 shows which herbs can inhibit CYP2C8. Mechanisms of herb-cancer drug interaction that can increase the concentration of cancer drugs in the bloodstream by decreasing their metabolism are shown in Table 3. Therefore, it is important to consider and avoid using combinations between herbs and cancer drugs that use CYP2C8 in the metabolism process. If it is necessary to use a combination, closely monitor any side effects.

Herbs have been reported to inhibit CYP2D6 (CYP2D6 inhibitors). Table 1 shows which herbs can inhibit CYP2D6. Mechanisms of herb-cancer drug interaction that can either increase or decrease the effectiveness of cancer drugs are shown in Table 3. As a result, it is important to consider and avoid using combinations between herbs and cancer drugs that use CYP2D6 in the metabolism process. If it is necessary to use a combination, closely monitor any side effects.

Herbs have been reported to inhibit UGT1A1 (UGT1A1 inhibition). Fa Thalai is an herb that can inhibit UGT1A1, as shown in Table 1. In vitro studies show their IC₅₀ is 5.00 µg/mL [18]. This herb can interact with cancer drugs that use UGT1A1 in the process of metabolism, especially etoposide, which uses UGT1A1 in glucuronidation [17]. The use of Fa Thalai in combination with etoposide contributes to a

high risk of interaction because the herb decreases the metabolism of etoposide and increases its concentration in the bloodstream. As a result, it is important to consider and avoid using combinations between Fa Thalai and cancer drugs that use UGT1A1 in metabolism. If it is necessary to use a combination, closely monitor any side effects.

Herbs have been reported to inhibit UGT2B7 (UGT2B7 inhibition). Fa Thalai is an herb that can inhibit UGT2B7, as shown in Table 1. In vitro studies show their IC₅₀ is 2.82 µg/mL [18]. This herb can interact with cancer drugs that use UGT2B7 in the metabolism, especially tamoxifen, which uses UGT2B7 in the glucuronidation process [19]. As a result, there is a high risk of interaction when using Fa Thalai with tamoxifen because the herb decreases its metabolism and increases drug plasma concentration. It is important to consider and avoid using combinations between Fa Thalai and tamoxifen. If it is necessary to use a combination, closely monitor any side effects.

Kwao Krua (*Pueraria mirifica*)

Kwao Krua contains substances that have estrogenic activity, such as deoxymiroestrol and miroestro. According to a report, this herb can inhibit the activity of tamoxifen citrate by competitively binding estrogen receptors and can decrease the effectiveness of contraceptives and estrogen therapy [20,21]. As a result, to decrease drug plasma concentration, avoid using Kwao Krua in patients receiving tamoxifen.

Garlic (*Allium sativum*)

Garlic can inhibit the activity of transferase and CYPs, especially docetaxel, which uses CYPs in metabolism. In studies showing interactions between garlic and docetaxel, garlic can decrease the elimination of docetaxel, but there is no significant difference in pharmacological interactions [22,23]. Garlic should therefore be avoided by patients receiving docetaxel.

Silymarin) *Silybum marianum*)

According to studies, silymarin is a component of flavonoids that can inhibit P-gp-mediated efflux in Caco-2 cells. Although vinblastine uses P-gp in the elimination process, silymarin also increases vinblastine levels in cells [26]. As a result, silymarin shouldn't be given to patients taking vinblastine.

In Thailand, there are a lot of cancer patients. According to reports, most cancer patients use herbs as supplements with their standard treatment. There is

currently no clear evidence that herbs can treat or be beneficial in the treatment of cancer. However, the risk of side effects from drug-herb interactions is increased when using a combination of herbs and cancer drugs. Although studies on these interactions have only been conducted in vitro, it is clear from pharmacological mechanisms that herbs can increase the likelihood of interactions between cancer drugs and herbs. Therefore, before using the herb while receiving the cancer drug, it is recommended to consult a doctor.

3. DIGITAL PLATFORM DESIGN FOR HERB-DRUG INTERACTION

The architecture of herb-drug interaction digital platform for cancer healthcare consists of web application, database system, and knowledge management system for herb-drug interaction as shown in Figure 1

We can categorize platform users based on their status and usage rights as follows: 1) General users have the privilege to view posts, ask questions, like posts, and search for information on herb-drug interaction. 2) Member group has the privilege to post articles, access posts, reply to posts, like posts, search for information on herb-drug interaction, participate in forum discussions, and create case reports. 3) Staff members have the privilege to post articles, access posts, reply to posts, like posts, search for information on herb-drug interaction, participate in forum discussions, and create case reports, add herb-drug interactions, create forums. 4) Administrators have the privilege to manage article posts, handle herb-drug interactions database, manage user accounts, oversee focus group data, manage drug information, manage herb information, administer forums, and oversee case reports.

Addition of Herb-Drug Interactions

You can create Herb-Drug Interaction data by following these steps: Go to the "Interaction" menu. Then, click on "Add New." and the system will display a form for drug management, as shown in Figure 2.

The details for herb management, as shown in Figure 3, include the following fields: effects, mechanism of Interaction, severity, onset (rapid/delayed), documentation, management, category, public description, warning categories, and references.

Once the staff members have entered herb-drug interaction data into the system's database, we can choose to match drugs with herbs to access herb-drug interaction information as shown in Figure 4.

Table 1 Herb that influences each enzyme in metabolism.

Pharmacological effects	Herbs
CYP3A4 inhibitor	Sweet fennel (<i>Foeniculum vulgare</i>), Jiaogulan <i>Gynostemma pentaphyllum</i> (, Black Galanga (<i>Kaempferia parviflora</i>), Bael fruit (<i>Aegle marmelos</i>), Garlic (<i>Allium sativum</i>), Dill (<i>Anethum graveolens</i>), Betel nut <i>Areca catechu</i> (, Caraway (<i>Carum carvi</i>), Tree basil (<i>Ocimum gratissimum</i> L.), Tumeric (<i>Curcuma longa</i>), Lotus (<i>Nelumbo nucifera</i>), Black cumin (<i>Nigella sativa</i>), Cat's whisker (<i>Orthosiphon aristatus</i>), Anise (<i>Pimpinella anisum</i>), Black pepper (<i>Piper nigrum</i>), Ringworm bush (<i>Senna alata</i>), Ajowan (<i>Trachyspermum ammi</i>), Phlai (<i>Zingiber cassumunar</i>)
CYP3A4 inducer	Dong Quai (<i>Angelica sinensis</i>)
CYP2C8 inhibitor	Jiaogulan
CYP2D6 inhibitor	Sweet fennel, Jiaogulan, Black Galanga, Garlic, Mo-noi (<i>Vernonia cinerea</i>), Lotus, Cat's whisker, Ringworm bush, Laurel clock vine (<i>Thunbergia laurifolia</i>)
UGT1A1 inhibition	Fa thalai (<i>Andrographis paniculata</i>)
UGT2B7 inhibition	Fa Thalai
Phytoestrogen	Kwao Krua (<i>Pueraria mirifica</i>)
Flavonoids (silybin, isosilybin, silychristin, silydianin)	Silymarin (<i>Silybum marianum</i>)

Table 2 Metabolite in each cancer drug.

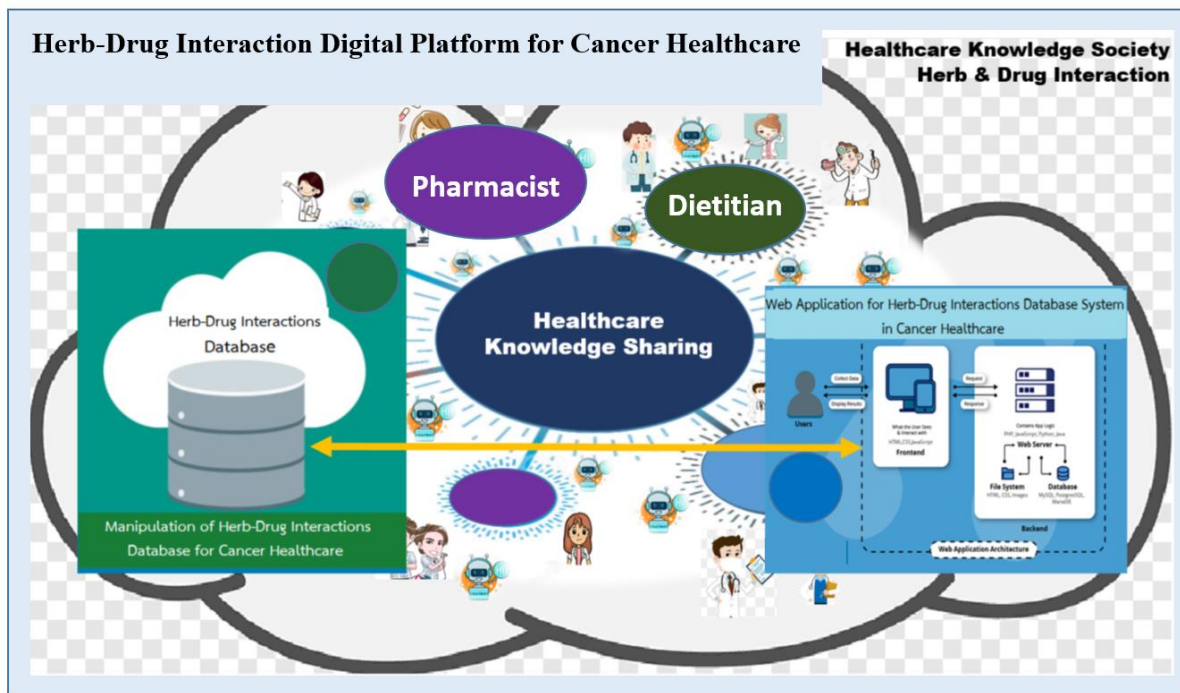
Substrate	Cancer drugs	Metabolites	
		Activated	Inactivated
CYP3A4 (major) ^[7]	Dasatinib	-	1) Hydroxylation at the para-position of the chloromethylphenyl ring (major metabolite) 2) Hydroxylation of the C5-methyl of the chloromethylphenyl ring 3) N-dealkylation of the hydroxyethyl moiety Hydroxy docetaxel
	Docetaxel	-	Doxorubicinol deoxyglycone
	Doxorubicin	-	-
	Etoposide	Etoposide catechol	-
	Imatinib	-	N-demethylated piperazine derivative (less active)
	Nilotinib	-	Oxidation and hydroxylation metabolites (less active)
	Paclitaxel	-	1) 3'-p-hydroxypaclitaxel 2) 6a,3'-p-dihydroxypaclitaxel
CYP3A4 (major) ^[7]	Vinblastine	Desacetyl vinblastine (more active)	-
	Vincristine	-	Dihydrohydroxycatharanthine vincristine derivative
	Ifosfamide	4-hydroxy derivatives	-
	Tamoxifen	1) Endoxifen 2) 4-hydroxytamoxifen	-
CYP2D6 (major)	Doxorubicin	-	Doxorubicin semiquinone ^[8]
	Tamoxifen	4-hydroxytamoxifen ^[9]	-
CYP2D6 (minor)	Vinblastine	Desacetyl vinblastine (more active)	-
CYP2C8 (major)	Paclitaxel	-	6-hydroxypaclitaxel ^[10]
P-glycoprotein/ABCB1 (minor)	Vinblastine	-	-
UGT1A1	Etoposide	-	Etoposide glucuronide ^[11]
UGT2B7	Tamoxifen	-	4-hydroxytamoxifen-O-glucuronide ^[12]

Table 3 Herb-cancer drug interactions.

Herb	Drug group	Interaction effects	Mechanism of interaction	Management	Description
CYP3A4 inhibitor	Substrate of CYP3A4 (Activated)	Increase drug concentration	The inhibition of CYP3A4 can lead to decreased metabolism and increased plasma drug concentration.	Avoid using combinations. If it is necessary, closely monitor any side effects.	Herbs can increase plasma drug concentrations and may cause more side effects.
	Substrate of CYP3A4 (Inactivated)	Decrease active metabolite levels	The inhibition of CYP3A4 can lead to decreased metabolism of active metabolites and thus decreased plasma drug concentration.		Herbs can affect drug activity and may cause less effectiveness.
CYP3A4 inducer	Substrate of CYP3A4 (Activated)	Increase active metabolites levels	The induction of CYP3A4 can lead to increased metabolism of active metabolites and thus increased plasma drug concentration and activity.	Avoid using combinations. If it is necessary, closely monitor any side effects.	Herbs can increase plasma drug concentrations and may cause more side effects.
	Substrate of CYP3A4 (Inactivated)	Decrease drug concentration	The induction of CYP3A4 can lead to increased metabolism and decreased plasma drug concentration.		Herbs can affect drug activity and may cause less effectiveness.
CYP2C8 inhibitor	Substrate of CYP3A4 (Activated)	Increase drug concentration	The inhibition of CYP2C8 can lead to decreased metabolism and thus increased plasma drug concentration.	Avoid using combinations. If it is necessary, closely monitor any side effects.	Herbs can increase plasma drug concentrations and may cause more side effects.
CYP2D6 inhibitor	Substrate of CYP2D6 (Activated)	Increase drug concentration	The inhibition of CYP2D6 can lead to decreased metabolism and thus increased plasma drug concentration.	Avoid using combinations. If it is necessary, closely monitor any side effects.	Herbs can increase plasma drug concentrations and may cause more side effects.
	Substrate of CYP2D6 (Inactivated)	Decrease active metabolite levels	The inhibition of CYP2D6 can lead to decreased metabolism of active metabolites and thus decreased plasma drug concentration and activity .		Herbs can affect drug activity and may cause less effectiveness.
UGT1A1 inhibition	Substrate of UGT1A1 (Inactivated)	Increase Etoposide concentration	Fa Thalai can inhibit UDP-glucuronosyltransferase 1A1 (UGT1A1) activity, which can lead to decreased metabolism and thus increased plasma drug concentration.	Avoid using combinations. If it is necessary, closely monitor any side effects.	Fa Thalai can increase plasma drug concentrations and may cause more side effects.
UGT2B7 inhibition	substrate of UGT2B7 (Inactivated)	Increase Tamoxifen concentration	Fa Thalai can inhibit UDP-glucuronosyltransferase 2B7 (UGT2B7) activity, which can lead to decreased metabolism and thus increased plasma drug concentration.	Avoid using combinations. If it is necessary, closely monitor any side effects.	Fa Thalai can increase plasma drug concentrations and may cause more side effects.

Table 3 Herb-cancer drug interactions) continue.(

Herb	Drug group	Interaction effects	Mechanism of interaction	Management	Description
Kwao Krua (<i>Pueraria mirifica</i>)	Tamoxifen citrate	Decrease Tamoxifen citrate levels	Kwao Krua can inhibit the activity of tamoxifen citrate by competitively binding estrogen receptors and can decrease the effectiveness of contraceptives and estrogen therapy.	Avoid using Kwao Krua in patients receiving tamoxifen.	Kwao Krua can decrease tamoxifen activity.
Garlic (<i>Allium sativum</i>)	Docetaxel	Increase Docetaxel concentration	Garlic can inhibit CYP activity, which can lead to decreased metabolism and thus increased plasma drug concentration.	Avoid using garlic in patients receiving docetaxel.	Garlic can increase plasma drug concentrations of docetaxel.
Silymarin (<i>Silybum marianum</i>)	Vinblastine	Increase Vinblastine concentration	Vinblastine is a P-gp substrate, whereas silymarin can inhibit P-gp-mediated efflux, thus increasing plasma drug concentration.	Avoid using combinations. If it is necessary, closely monitor any side effects.	Flavonoids in silymarin can increase the adsorption of vinblastine.

**Figure 1.** The Architecture of Herb-Drug Interaction Digital Platform

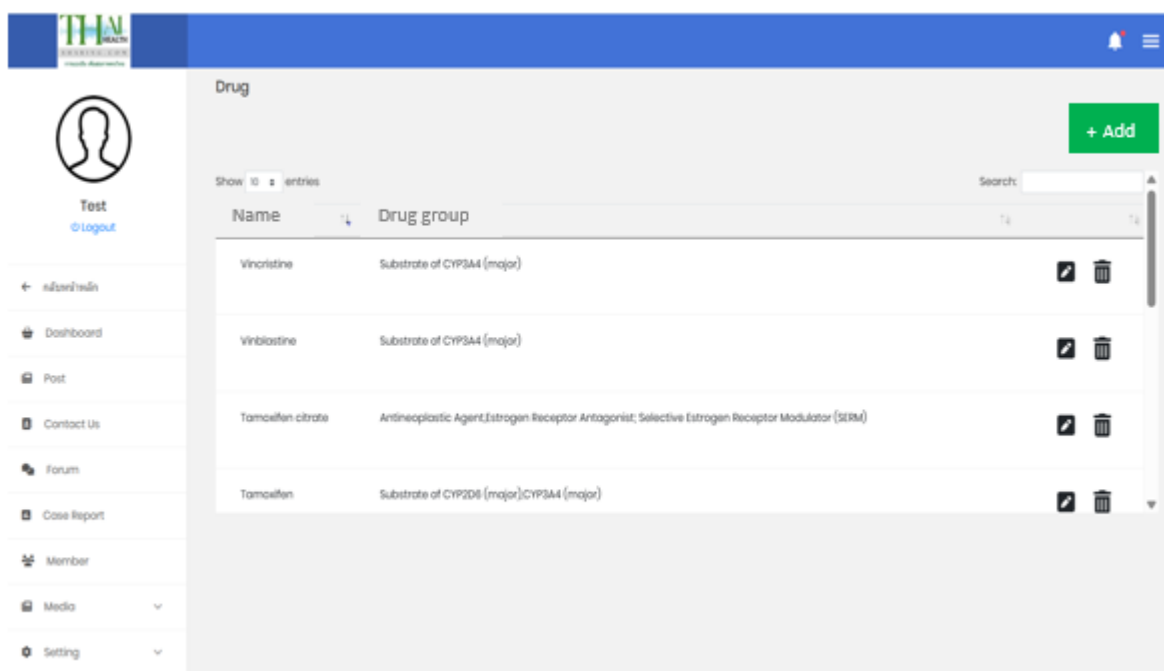


Figure 2. Drug Management Window

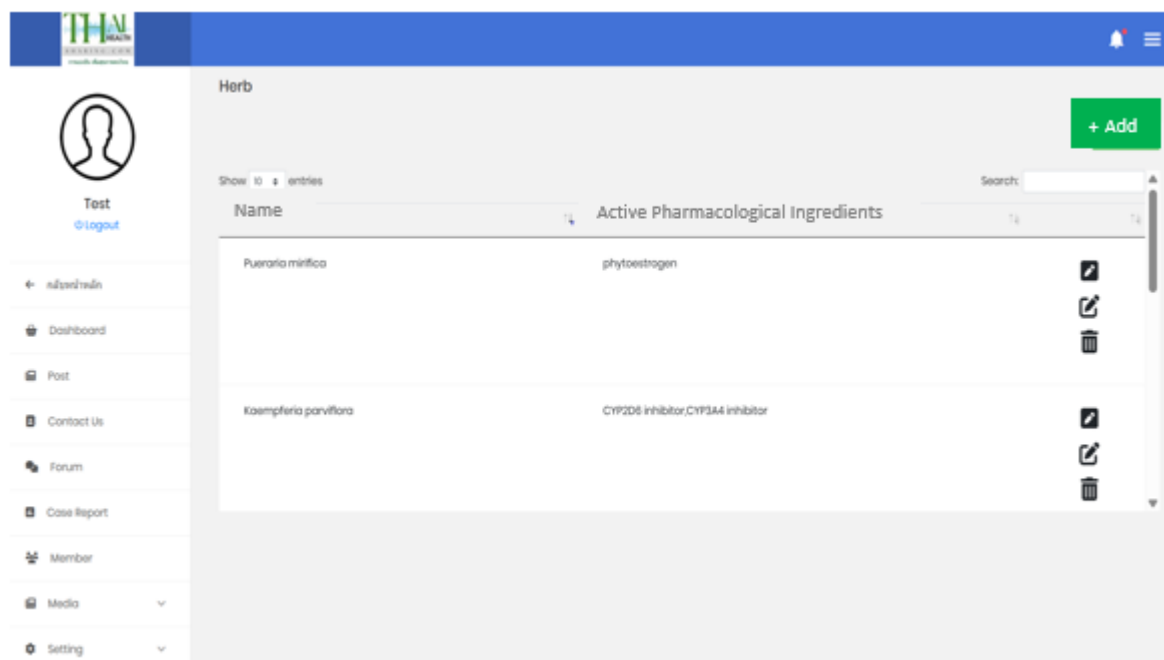


Figure 3. Herb Management Window



THAI HEALTH
SHARING.COM
แลกเปลี่ยน เพื่อสุขภาพไทย

Herb-Drug Interactions for Cancer Healthcare

--Drug--

--Herb--

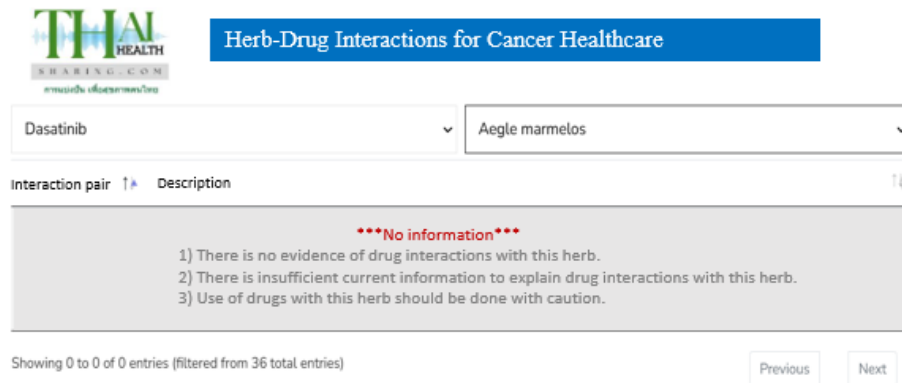
Interaction pair	Description
 Aegle marmelos  Imatinib	ผล (Effects) Increase concentrations of anticancer drug กลไกการเกิดอันตรกิริยา (Mechanism of interaction) Aegle marmelos inhibits CYP1A2 activity, which may decrease drug metabolism. A study found that the methanolic extract of Aegle marmelos inhibited CYP1A2 with an IC50 value of 0.8 µg/mL. Severity N/A Documentation (Reliability of the data, such as whether it comes from case reports or clinical trials.) In vitro study Management Consider avoiding concomitant use or, if necessary, closely monitor for adverse effects. Explanation for the public Bael fruit extract may increase blood levels of this drug, which may increase side effects. คำเตือน (Warning) Consider changing your medication or closely monitor for side effects. Reference

Figure 4. Example of Herb-Drug Matching

In case there is no matching between a drug and a herb, the system will display drug-specific warning information, as shown in Figure 5. However, if you want to see more details about an herb, click on the herb's image or the herb's name. The system will display all the available details for you to read.

The system has prepared a feature to facilitate staff or members to report and record Case Reports of

using medications in conjunction with herbs. This is intended to be beneficial for discussions, knowledge exchange in forums, and future research. The menu and form for entering case reports will include interaction pair, symptoms description, severity, evidence or supporting data, guidelines for resolution, gender, age, chronic conditions, additional Information as shown in Figure 6.



THAI HEALTH
SHARING IS Caring

Herb-Drug Interactions for Cancer Healthcare

Dasatinib Aegle marmelos

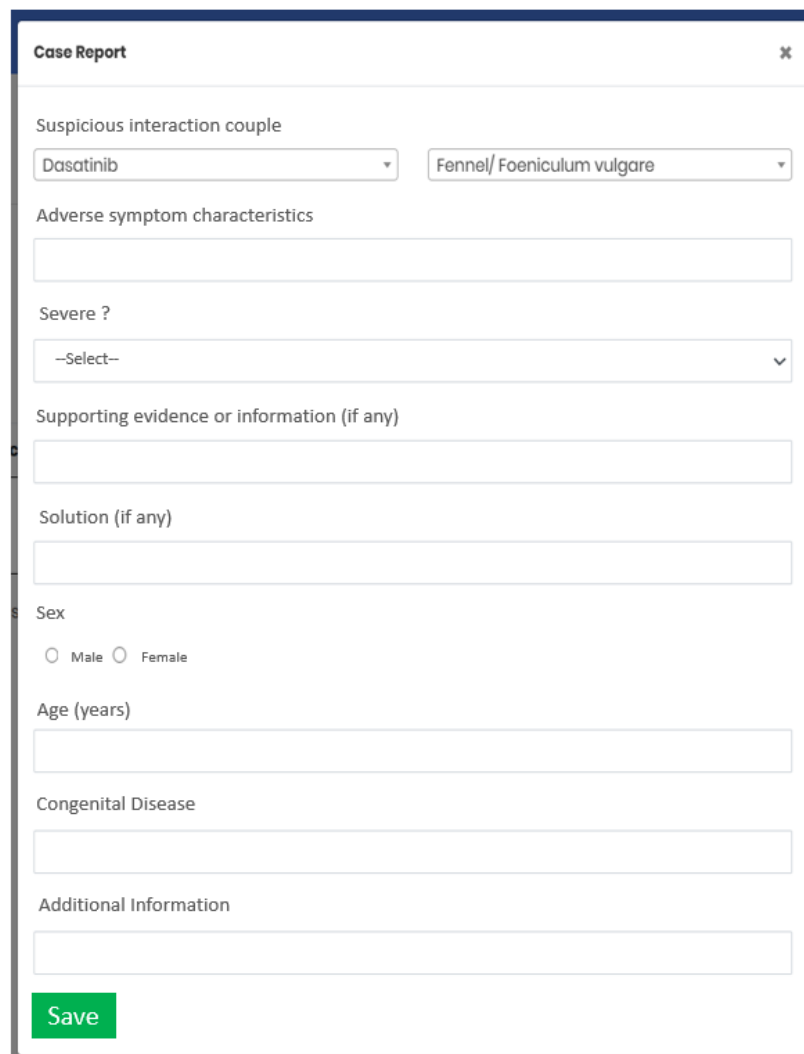
Interaction pair Description

*****No information*****

- 1) There is no evidence of drug interactions with this herb.
- 2) There is insufficient current information to explain drug interactions with this herb.
- 3) Use of drugs with this herb should be done with caution.

Showing 0 to 0 of 0 entries (filtered from 36 total entries) Previous Next

Figure 5. Results of Matching a Drug and a Herb When No Match is Found.



Case Report

Suspicious interaction couple

Dasatinib Fennel/ Foeniculum vulgare

Adverse symptom characteristics

Severe ?

—Select—

Supporting evidence or information (if any)

Solution (if any)

Sex

☐ Male ☐ Female

Age (years)

Congenital Disease

Additional Information

Save

Figure 6. Case Report Form

4. PLATFORM TESTING

This herb-drug interaction platform has been tested according to the designed functions through automated testing using the Selenium IDE program with various test cases. The results indicate that the platform performed as designed as shown in Table 4.

Table 4 Platform Testing Results

Test	Test Cases	Status
1.	Login : End user/Member/Staff/Admin	√
2.	Manage/Add/Public/Edit/Delete/Reply to the Post	√
3.	Add/Edit/Delete the Herb-Drug Interaction	√
4.	Manage/Add/Edit/Delete the User	√
5.	Focus group management : In case of a match found /In case of no match found	√
6.	Manage/Add/Edit/Delete the Drug	√
7.	Manage/Add/Edit/Delete the Herb	√
8.	Manage/Add/Edit/Delete the Forum	√
9.	Manage/Add/Edit/Delete the Case Report	√

5. CONCLUSION

From the design and development of herb-drug interaction digital platform for cancer healthcare in this research, it can be summarized that the system consists of three subsystems: web application, herb-drug interactions database system, and knowledge management system for herb-drug interaction. When considering the herb-drug interaction database, it comprises the following components: effects, mechanism of interaction, severity, onset (rapid/delayed), documentation, management, category, public description, warning categories, and references. The objective is to serve as a knowledge hub, database, healthcare assistance tool, and a vital and beneficial community for knowledge exchange among healthcare professionals, patients, and the general public. In this research, the database on herb-drug interaction comprises drug name, pharmacological group, herb name, active ingredient/pharmacological properties, effects, mechanism of interaction, severity, documentation,

management, patient-friendly explanation, warning categories, and references. This platform will help address the issue of using herbal remedies in conjunction with current pharmaceutical treatments, which can potentially pose risks to users, especially when interactions between drugs and herbs may occur gradually and go unnoticed until patients experience harm or severe adverse effects on their health. From the digital platform testing conducted in this research using automated testing with Selenium IDE and various test cases, it was found that the system operates correctly in accordance with the designed functions in all aspects.

However, the herb-drug interaction database must continue to be updated and expanded to include comprehensive information on all types of medications and herbs. Researchers can use data from case reports that members have recorded on this platform to analyze, study, and generate new herb-drug interactions. Subsequently, this new information can be added to the platform, benefiting medical professionals and the general public for future knowledge retrieval.

6. ACKNOWLEDGEMENTS

This research was funded by Thailand Science Research and Innovation via Srinakharinwirot University (Grant number 014/2566). We would like to thank the Faculty of Medicine, Faculty of Engineering, Srinakharinwirot University, Chulabhorn Royal Pharmaceutical Facilities, Chulabhorn Royal Academy, and College of Medicine and Public Health, Ubon Ratchathani University, Thailand for supporting this research until it was successfully completed.

REFERENCES

- [1] Yekta Z., Ebrahimi S., Hosseini M., Nasrabadi A., Sedighi S., Surmaghi M.Madani H. (2012). Ginger as a miracle against chemotherapy-induced vomiting. Iran J Nurs Midwifery, 17(5):325-9.
- [2] Nuntapong Boonrit. (2018). Impact of Ontogeny on Pharmacokinetics and Pharmacodynamics in Pediatric Patients, Thai Journal of Pharmacy Practice, 10(2), 463-474.
- [3] Wu, J., Guan, X., Dai, Z., He, R., Ding, X., Yang, L., & Ge, G. (2021). Molecular probes for human cytochrome P450 enzymes: Recent progress and future perspectives. Coordination Chemistry Reviews, 427.

- [4] Akekamon Piboonwattanapong. (2018). Systemic therapy. Retrieved August 10, 2023, from https://www.chularat3.com/knowledge_detail.php?lang=th&id=455
- [5] Panupong Putharak. (n.d.). Retrieved August 10, 2023, from <https://ccpe.pharmacycouncil.org/showfile.php?file=400>
- [6] Srinagarind Medical Journal. (n.d.). Retrieved August 10, 2023, from http://www.smj.ejnal.com/e-journal/showdetail/?show_detail=T&art_id=1380
- [7] Sornsuvit, C., Phosuya, C., Jaronwanichkul, D., & Piriyananusanorn, N. (2012). The Use of Herbal and Dietary Supplements and Potential Interactions with Drugs in Patients with Chronic Diseases. *Thai Pharmaceutical and Health Science Journal*, 7(4), Article
- [8] McCune, J. S., Hatfield, A. J., Blackburn, A. A. R., Leith, P. O., Livingston, R. B., & Ellis, G. K. (2004). Potential of chemotherapy-herb interactions in adult cancer patients. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, 12(6), 454–462. <https://doi.org/10.1007/s00520-004-0598-1>
- [9] Yu, C., Chai, X., Yu, L., Chen, S., & Zeng, S. (2011). Identification of novel Pregnane X receptor activators from traditional Chinese medicines. *Journal of Ethnopharmacology*, 136(1), 137–143. <https://doi.org/10.1016/j.jep.2011.04.022>
- [10] Regina A., Jan N.M. C., Civianny A., Nico P.E. V. (2008). Interactions between cytochromes P450, glutathione S-transferases and Ghanaian medicinal plants. *Food and Chemical Toxicology*. <https://doi.org/10.1016/j.fct.2008.09.002>.
- [11] Jiso, A., Khemawoot, P., Techapichetvanich, P., Soopairin, S., Phoemsap, K., Damrongsakul, P., Wongwiwatthanankit, S., & Vivithanaporn, P. (2022). Drug-Herb Interactions among Thai Herbs and Anticancer Drugs: A Scoping Review. *Pharmaceuticals*, 15(2), 146. <https://doi.org/10.3390/ph15020146>
- [12] Qsbplant-db. (n.d.). QSBG Database. Retrieved July 10, 2023, from <http://www.qsbg.org/Database/plantdb/mdp/hbmdetails.asp?id=463>
- [13] Pouyfung, P., Saraputit, S., & Rongnoparut, P. (2017). Effects of Vernonia cinerea Compounds on Drug-metabolizing Cytochrome P450s in Human Liver Microsomes. <https://onlinelibrary.wiley.com/doi/10.1002/ptr.5939>
- [14] Ye, L. H., Kong, L. T., Yan, M. Z., Cao, F. R., Wang, L. S., Liao, Y. H., Pan, R. L., & Chang, Q. (2016, October 19). Lotus leaf alkaloid fraction can strongly inhibit CYP2D6 isoenzyme activity. *Journal of Ethnopharmacology*. <https://www.sciencedirect.com/science/article/abs/pii/S0378874116314295?via%3Dihub>
- [15] Ye, L. H., He, X. X., Kong, L. T., Liao, Y. H., Pan, R. L., Xiao, B. X., Liu, X. M., Chang, Q., Subehan, Takahashi, N., Usia, T., Chan, E., Du, H., & Fan, T. (2014, February 21). Identification and characterization of potent CYP2D6 inhibitors in Lotus leaves. *Journal of Ethnopharmacology*. <https://www.sciencedirect.com/science/article/abs/pii/S0378874114001159?via%3Dihub>
- [16] Pan, Y., Rashid, B. A. A., Ismail, Z., Ismail, R., Mak, J. W., Pook, P. C. K., Er, H. M., & Ong, C. E. (2011, January 27). In vitro effects of active constituents and extracts of orthosiphon stamineus on the activities of three major human cDNA-expressed cytochrome P450 enzymes. *Chemico-Biological Interactions*. <https://www.sciencedirect.com/science/article/abs/pii/S0009279711000469?via%3Dihub>
- [17] Wen, Z., Tallman, M. N., Ali, S. Y., & Smith, P. C. (2007). UDP-glucuronosyltransferase 1A1 is the principal enzyme responsible for etoposide glucuronidation in human liver and intestinal microsomes: structural characterization of phenolic and alcoholic glucuronides of etoposide and estimation of enzyme kinetics. *Drug metabolism and disposition: the biological fate of chemicals*, 35(3), 371–380. <https://doi.org/10.1124/dmd.106.012732>
- [18] Ismail, S., Aziah Hanapi, N., Ab Halim, M. R., Uchaipichat, V., & Mackenzie, P. (2010). Effects of Andrographis paniculata and Orthosiphon stamineus Extracts on the Glucuronidation of 4-Methylumbelliferone in Human UGT Isoforms. *Molecules*, 15(5), 3578–3592. <https://doi.org/10.3390/molecules15053578>
- [19] Hao, Z., Xu, J., Zhao, H., Zhou, W., Liu, Z., He, S., Yin, X., Zhang, B., Wang, Z., & Zhou, X. (2022). The inhibition of tamoxifen on UGT2B gene expression and enzyme activity in rat liver contribute to the estrogen homeostasis dysregulation. *BMC pharmacology & toxicology*, 23(1), 33. <https://doi.org/10.1186/s40360-022-00574-6>
- [20] Stansbury, J., Saunders, P. R., & Winston, D. (2013). The Safety of Phytoestrogens in Menopause, Prostate and Breast Cancer. *Journal of Restorative Medicine*, 2(1), 101. <https://doi.org/10.14200/jrm.2013.2.0110>
- [21] Oseni, T., Patel, R., Pyle, J., & Jordan, V. C. (2008). Selective estrogen receptor modulators and phytoestrogens. *Planta Medica*, 74(13), 1656–1665. <https://doi.org/10.1055/s-0028-1088304>

- [22] Cox, M. C., Low, J., Lee, J., Walshe, J., Denduluri, N., Berman, A., Permenter, M. G., Petros, W. P., Price, D. K., Figg, W. D., Sparreboom, A., & Swain, S. M. (2006). Influence of garlic (*Allium sativum*) on the pharmacokinetics of docetaxel. *Clinical cancer research : an official journal of the American Association for Cancer Research*, 12(15), 4636–4640. <https://doi.org/10.1158/1078-0432.CCR-06-0388>
- [23] Fasinu, P. S., & Rapp, G. K. (2019). Herbal Interaction With Chemotherapeutic Drugs-A Focus on Clinically Significant Findings. *Frontiers in oncology*, 9, 1356. <https://doi.org/10.3389/fonc.2019.01356>
- [24] Zhang, S., & Morris, M. E. (2003). Effect of the flavonoids biochanin A and silymarin on the P-glycoprotein-mediated transport of digoxin and vinblastine in human intestinal Caco-2 cells. *Pharmaceutical research*, 20(8), 1184–1191. <https://doi.org/10.1023/a:1025044913766>
- [25] Kimura, Y., Ito, H., & Hatano, T. (2010). Effects of Mace and Nutmeg on Human Cytochrome P450 3A4 and 2C9 Activity. *Biological and Pharmaceutical Bulletin*, 33(12), 1977–1982. <https://doi.org/10.1248/bpb.33.1977>



Watchara Kanjanakawinkul received his B.Pharm. and Ph.D. in Research and Development in Pharmaceuticals from the Faculty of Pharmaceutical Sciences, Khon Kaen University, Thailand, in 2006 and 2013, respectively. He has been involved in the pharmaceutical industry since 2006 and began his academic career as a lecturer at the Faculty of Pharmacy, Burapha

University, Thailand, in 2013. In 2014, he joined the National Biopharmaceutical Facility at King Mongkut's University of Technology Thonburi as a product manager. Currently, he serves as the Director of the Chulabhorn Royal Pharmaceutical Facility at the Chulabhorn Royal Academy. His research interests include drug formulation, drug delivery systems, drug development, anticancer, sterile product, and the pharmaceutical industry.



Kamon Chaiyasit received MSc in Pharmacology from Chulalongkorn University Thailand (2007), PhD in Nutrition from USA (2012) and Bachelor of Law and PhD in Innovation Communication in Political and Local administration from STOU, Thailand (2020), Palliative care in hospitalist and internist from Harvard Medical School and Fellow of American College of Nutrition. He holds

American Board Certified in Nutritional Wellness. He is a President of Integrative Nutrition and Herbal Medicine Association. He works at Integrative Cancer Center at Esperance Clinic Bumrungrad International hospital.



Maethaphan Kitporntheranunt received the M. D. from Faculty of Medicine, Chiang Mai University, Thailand in 1997. In 2001 he joined the Faculty of Medicine, Srinakharinwirot University, Thailand, as an instructor where he became an Associate Professor in 2018. He had research experience/subspecialty training at King Chulalongkorn Memorial Hospital, Thailand and KK Women's and Children's Hospital, Singapore in 2003 and 2009 respectively. His interests include Medical Education, Medical Instrument and Innovation, Health Technology and Medical Expert System.



Watcharachai Wiriyasuttiwong received the B.Eng. in Electrical Engineering from Prince of Songkha University (PSU), Thailand in 1994., M.Eng. in Electrical Engineering, Distinguished Thesis, Chiangmai University in 1999. Currently, he is a Assistant Professor in Department of Computer Engineering, Faculty of Engineering at

Srinakharinwirot University (SWU), Thailand. His interests include AI, Machine Learning, Knowledge Engineering and Fuzzy Expert System.



Latiporn Udomsuk received the B.Pharm. in Pharmaceutical Sciences in 2007, M.Pharm in Pharmaceuticals in 2009, and Ph.D. in Research and Development of Pharmaceuticals in 2012 from Khon Kaen University (KKU), Thailand. Currently, she is an Assistant Professor in Department of Preclinical Science, College of Medicine and Public Health at Ubon Ratchathani University

(UBU), Thailand.



Sorawuth Pongrojphao received the M.D. from Faculty of Medicine, Ramathibodi hospital, Mahidol University, Thailand in 1991. In 1997 he joined the Faculty of Medicine, Srinakharinwirot University, Thailand, as an instructor. Currently, he is a Assistant Professor in Department of Pediatrics, Faculty of Medicine at Srinakharinwirot University (SWU), Thailand.