Mitigating the Impact of Admixtures in Thai Herbal Products

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Medicinal plants and their products are extensively used within indigenous healthcare systems in Thailand and several other nations. The international trade of herbal products has a noteworthy impact on the worldwide economy, and the interest in herbal products is expanding in both developing and developed countries. There has been rapid growth in the medicinal plant product market and a broadening consumer base interested in herbal products from Thailand. However, in herbal industries, ingredient substitution and admixture are typical issues wherein species of lower market value are admixed with those of a higher value. The adverse consequences of consuming adulterated drugs are invariably due to the presence of an unintended herb rather than the presence of an intended herb. It has also been argued that admixtures are intentional because of the lack of regulatory policies or centralized tests for product authentication. The consequences of species admixtures can extend from the reduced efficacy of a drug to decreased trade value. This study aims to clarify the nature and extent of species admixtures reported in the Thai herbal trade market and discuss the potential reasons for such adulteration. In the broader context of species admixtures, we strongly propose the establishment of multiple herbal crude drug repositories that can be developed to facilitate the use of comparative identity tests by industry, traders, and researchers to maintain authentic natural health product (NHP) standards and to certify the authenticity of NHPs. The proposition of the establishment of centralized testing (CT) could be a promising initiative in Thailand for the development of science and technology, and the herbal medicines produced as a result of CT could be dispensed as prescription drugs based on disease consideration instead of as health foods or nutraceuticals.

Keywords: admixtures, adulterations, medicinal plants, Thai herbal products, herbal database

INTRODUCTION

Medicinal plants contribute significantly to both the indigenous and modern systems of medicine. Since ancient times, medicinal plants have been used in traditional home remedies and have formed a major component of the indigenous system of medicine practiced in many countries. It has been reported that 80% of the world’s population depend on traditional herbal medicines, mainly plant-based herbal drugs, for their primary healthcare (Srirama et al., 2017). The international trade of medicinal plants and their herbal products contributes to the worldwide economy; thus, the demand for such herbal products is growing in both developing and developed countries. More than 28,187 species of plants are used for medicinal purposes (Medicinal Plant Names Services Portal, 2017).
These plants are used as either herbal medicines by the indigenous and rural communities or in the manufacture of pharmaceutical drugs. Currently, there are more than 1,000 herbal companies producing medicinal plant products, and their annual income is in excess of $60 billion (Newmaster et al., 2013). Due to commercialization and increased demand for traditional herbs, safety, quality, and assurance are major issues (Chen et al., 2017).

In recent years, an international resurgence of attention has occurred in the use of herbal products in human healthcare, which has led the herbal product market to thrive (Barry and Abratt, 2015). The increase in demand has far outpaced the availability of raw materials. Thailand's major exports of medicinal plants are used in pharmaceutical, perfumery, etc. Estimated exports of herbal products from Thailand indicate an increase from US$1.4 million in 2007 to US$11.5 million in 2011, recording a compounded annual growth rate of 12.67%. The major export markets of Thai herbal extracts are Myanmar (38.72%), the United States (13.15%), Cambodia (10.92%), Japan (9.50%), the United Kingdom (6.79%), and Hong Kong (3.31%), whereas the import markets include China, Brazil, the United States, Germany, Philippines, and India (https://report.nat.gov.tw). However, due to high demands, the substitution and adulteration of many medicinal plant species in medicinal plant products (Techen et al., 2004; Song et al., 2009; Suwanchaikasem et al., 2013; Urumarudappa et al., 2016; Srirama et al., 2017; Dechbhumroong et al., 2018; Kumar et al., 2018), breweries such as teas (Stoeckle et al., 2011), and “nutraceuticals” (Bruni et al., 2010; Jaakola et al., 2010) have been documented.

Medicinal plants used in raw herbal trade are often marketed as powders; dry twigs including dry roots, rhizomes, leaves, etc.; and pills or tablets, and thus are usually difficult to identify morphologically. The major problems with the trade of raw herbal products include the adulterations and substitution of certain species with morphologically similar and geographically co-occurring species (Ved and Goraya, 2007; Urumarudappa et al., 2016; Srirama et al., 2017). In most of the Southeast Asian countries, including Thailand, over 80% of the medicinal plants that are in active trade are seldom cultivated. These are collected largely from the wild. The collection of these medicinal plants is largely performed by local people who often rely only on their knowledge or experience in identifying the species being collected (Menon, 2003; Seethapathy et al., 2015; Srirama et al., 2017). Thus, most often, there are admixtures of related species or morphologically similar species in the herbal trade samples. The possible reasons for adulteration are often attributed to the apparent confusion associated with local or vernacular names of plant species, lack of accurate raw plant material, and identical morphological characters of co-occurring species of plants (Mitra and Kannan, 2007; Kumar et al., 2018). Admixture is a common malpractice in raw material trade and a major problem in the herbal industry. Admixture is the practice of substituting an authentic crude drug partially or entirely with a different drug similar to the original drug but inferior in therapeutic and synthetic properties or the addition of low-efficiency drugs for the intentional or unintentional enrichment of profits (Mukherjee, 2002; Kokate et al., 2007). The adverse consequences of consuming adulterated drugs are invariably due to the presence of an unintended herb rather than the presence of an intended herb (Sunita, 1992; Uniyal and Joshi, 1993; Sarin, 1996). It has also been argued that admixture is deliberate because there is no standard monitoring tool in place or commercial test for product authentication. The consequences of species admixtures can extend from the reduced efficiency of a drug to the decreased trade value (Wieniawski, 2001), in addition to a threat to the safety of consumers (Song et al., 2009).

Since adulteration is very difficult to trace in situ and requires expertise, scientific methods have been developed to address medicinal plant adulteration in herbal trade, such as microscopic, macroscopic, organoleptic, and chemical analyses (Techen et al., 2014; Moraes et al., 2015; Mishra et al., 2016; Pawar et al., 2017; Raclariu et al., 2018). DNA technology has been heavily used to investigate the adulteration of species (Newmaster et al., 2013; Phoolcharoen and Sukrong, 2013; Kumar et al., 2015; Urumarudappa et al., 2016; Pawar et al., 2017; Dechbhumroong et al., 2018; Liu et al., 2018; Raclariu et al., 2018; Seethapathy et al., 2018; Speranskaya et al., 2018; Kreuzer et al., 2019). Among the available tools for species identification and traceability, DNA barcoding is a low-cost and highly efficient approach that has the potential for automatization and rapid application (Galimberti et al., 2013; Mishra et al., 2016; Dechbhumroong et al., 2018).

In this review, we attempt to elucidate the nature and extent of species adulteration reported in the Thai herbal trade market and discuss the possible underlying causes of adulteration. In the larger context of species admixtures, we believe and propose the need to certify the centralized system to develop an efficient mechanism to systematically evaluate traditional medicine and connect it with both national and international trade regulators. We strongly suggest the establishment of several crude herbal drug depositories to maintain authentic biological reference materials (BRMs) that can be developed to facilitate the use of comparative identity tests by industry, traders, and researchers and to certify herbal product authenticity. We strongly recommend the enforcement of existing laws and regulations concerning the quality of herbal products to govern herbal trade around the globe. The proposed establishment of centralized testing (CT) could be a promising initiative in Thailand for the development of science and technology. The herbal medicines produced as a result of CT could be dispensed as prescription drugs based on disease consideration instead of being designated health foods or nutraceuticals. CT could pave the way to increase the country's market size of phytomedicine and become a novel strategy in Thailand as an important contributor to the herbal product market and to maintain the safety and health of consumers.

MATERIALS AND METHODS

Literature Search on Medicinal Plants Used in Thai Herbal Pharmacopoeia (THP)

In this study, the list of plants in Thailand Herbal Pharmacopoeia (THP) was the main focus. A literature search was performed with various electronic databases [Google Scholar, Science Direct
Origin of Thai Traditional Medicine (TTM)

Traditional medicines have been established after extensive experiences of over 100 years of practicing physicians in the indigenous systems of medicine (Kamboj, 2000). Traditional medicine of Thailand has an extensive history of use in various treatments and illnesses since the Sukhothai period (1238–1337) of Thai history. By the knowledge passed down through generations, a well-defined structure of traditional medicine has been developed, systematized, and is now recognized as Thai Traditional Medicine (TTM) by the Kingdom of Thailand (SEARO, WHO, 2010). TTM is considered holistic medicine, as it involves not only the use and production of herbal medicine but also diagnosis, treatment, and pharmacy practice (Akarasereenont et al., 2015). The famous Thai massage (Nuad Thai) also originates from this system.

TTM draws its traditional content from the Indian and Chinese systems (WHO, 2002), as indicated by the diversity of ethnic groups in Thailand’s population (Trisonthi and Trisonthi, 1995), possibly due to historic migration from neighboring countries (Phumthum and Balslev, 2018). Maintenance of unique and distinctive knowledge of medicinal plants has been seen mainly in these communities. Additionally, a study on a typical mountain-residing indigenous community named “Karen” showed that having limited access to public healthcare systems encouraged them to accumulate a valuable method of preventing and treating diseases with herbal remedies (Tangjitarian et al., 2015). However, TTM observed a decline in consumer acceptance from 1916 to 1977 due to the influence of Western medicine, although a subsequent revival in acceptance was observed after the WHO advised that traditional medicine and plant herbal medicine should be implemented in primary healthcare systems (Akarasereenont et al., 2015). Then, to accelerate the integration of traditional medicine into national healthcare system, a list of the national essential herbal drugs (NEHD) was established in 1999 according to the National Drug Committee (2006). Today, the Thai government also funds and strongly supports medicinal plant research and development.

To reduce the cost of imported drugs and improve access to healthcare, ASEAN members agreed to implement the WHO’s traditional medicine strategy (WHO, 2002) in the year 2004, which in turn enhanced the use of traditional medicine, especially herbal medicine, in ASEAN healthcare systems. A recent investigation reports that Thai people spend several million bahts per year on unproven herbal products (Osathanunkul et al., 2016). Currently, alternative medicines are popular not only in developing countries, such as Thailand and India, but also in developed countries, such as the United States, Canada, and Europe. In support of this, an estimate shows that the United States alone spends over US$5 billion per year on herbal products (Osathanunkul et al., 2016). However, herbal products are considered supplements rather than medicines in the United States, which may be due to the absence of clinical data on their safety and efficacy.

Species Admixtures in Herbal Trade: Thai Herbal Pharmacopoeia

THP has listed 66 medicinal plants with a high therapeutic index as herbal medicine (Table 1). This study considered the listed medicinal plants to understand their status under the threat of adulteration in herbal trade (Table 2). A previous report has shown that 15.5% of the total number of plant species in Thailand is used as medicinal plants (Wadikar, 2004). Recently, a number of studies have also shown that natural health product (NHP) market samples of raw herbal trade materials are often adulterated with other species (Kool et al., 2012; Newmaster et al., 2013; de Boer et al., 2015; Kumar et al., 2015; Urumuradappa et al., 2016; Mezzasalma et al., 2017; Pawar et al., 2017; Dechbumroong et al., 2018; Raclariu et al., 2018; Liu et al., 2018; Seethapathy et al., 2018; Speranskaya et al., 2018; Tunghathong et al., 2018; Kreuzer et al., 2019).

A number of studies have reported species admixtures in herbal trade across countries. For example, DNA-based approaches have been used for the identification of species listed in Amazonian traditional medicine (Mezzasalma et al., 2017). Trachelospermum jasminoides is commonly used as traditional Chinese medicine and sold in markets in dried and sliced forms, which pose difficulties in traditional identification methods. Yu et al. (2017) used the nuclear region ITS2 to evaluate the 127 sequences representing T. jasminoides via the neighbor-joining tree method, which demonstrated the remarkable use of DNA barcoding to authenticate market samples. Using the ITS2 region, Chen et al. (2017) found that only 78% of the market samples contained the species listed on their product label. A few studies showed the use of both molecular and chemical markers and phylogenetic approaches for the identification of herbal products, including dietary supplements. For example, a study using a phylogenomic approach analyzed the evolutionarily complex genus Berberis in order to develop DNA barcodes for the medicinally important species Berberis aristata for the regulatory purposes and quality control (Kreuzer et al., 2019).

The combination of molecular and chemical markers ensures the quality of the Copalchi complex used in Mexican Herbal Pharmacopoeia and successfully differentiates between the species Hintonia latiflora, H. standleyana, and Eostemma caribaeanum (Cristians et al., 2018). Pawar et al. (2017) used traditional DNA barcoding techniques and chemical markers to identify frequently consumed botanical dietary supplements of ginkgo, soy, valerian, yohimbe, etc. The combination of DNA barcoding and nuclear magnetic resonance (NMR) was used for the identification of admixture in Garcinia species (Seethapathy et al., 2018) and Saraca acosa (Urumuradappa et al., 2016). Wang et al. (2016) used DNA barcoding for the identification of processed Angelicae sinensis radix (Danggui) used in Chinese patent medicines (CPMs). Lonicerae japonicae Flos was used to produce hundred kinds of CPMs, single nucleotide polymorphisms (SNPs) were used to generate
| Thai name | Scientific name | Family | Habit | Parts used | Treatment/application |
|-----------|----------------|--------|-------|------------|-----------------------|
| Wannam   | Acorus calamus L. | Acoraceae | Aquatic perennial herb | Dried rhizome | Carminative |
| Matum    | Aegle marmelos (L.) Corrêa | Rutaceae | Tree | Fruits and bark | Antidiarrheal, stomachic |
| Horng    | Allium ascalonicum L. | Amaryllidaceae | Biennial herb | Dried bulb | Carminative, expectorant |
| Krathiam | Allium sativum L. | Amaryllidaceae | Herb | Bulb | Antimicrobial, antihyperlipidemic |
| Fa Thalai | Andrographis paniculata (Burm. f.) Nees | Acanthaceae | Herb | Dried aerial part | Antidiarrheal, antipyretic, antiinflammatory |
| Thian Ta Takkan | Anethum graveolens L. | Apiaceae | Annual herb | Dried ripe fruit | Carminative, medicinal aid |
| Kot      | Angelica dahurica (Hoffm.) Benth. & H | Apiaceae | Perennial herb | Dried root | Antipyretic, analgesic |
| Kot Chiang | Angelica sinensis (Oliv.) Diels | Apiaceae | Perennial herb | Roots | Blood tonic, treatment of mental disorders |
| Khamin Khrua | Arcangelisia flava (L.) Merr. | Menispermaceae | Large climber | Stem | Stomachic, antidiarrheal, antibacterial |
| Maksong  | Areca catechu L. | Areceae | Small or medium sized tree | Ripe seed | Antithrombotic, antidiarrheal |
| Kot Chula Lampha | Artemisia annua L. | Asteraceae | Annual herb | Dried aerial part | Antipyretic |
| Kot Khamao | Atractylodes lancea (Thunb.) DC. | Asteraceae | Perennial herb | Rhizome | Stomachic |
| Kot Kraduk | Aucklandia lappa Decne | Asteraceae | Herb | Roots | Stomachic, carminative, antispasmodic |
| Sawat    | Caesalpinia bonduc (L.) H. Roxb. | Fabaceae | Climber | Leaf | Laxative, antiflatulent |
| Phrik Khinu | Capsicum annuum L. | Solanaceae | Annual or perennial herb | Dried ripe fruit | Gastro-intestinal stimulant, counterirritant |
| Thian Ta Kop | Carum carvi L. | Apiaceae | Perennial herb | Dried ripe fruit | Carminative, antiflatulent, pharmaceutic aid |
| Khun     | Cassia fistula L. | Fabaceae | Tree | Leaf | Laxative |
| Buabok   | Centella asiatica (L.) Urb. | Apiaceae | Herb | Aerial part | Mild diuretic, antinflammatory, wound healing |
| Phet Sangkhut | Cissus quadrangularis L. | Vitaceae | Woody climber | Dried stem | Aleivation of hemorrhoidal symptoms |
| Makrut   | Citrus hystrix DC. | Rutaceae | Shrub or small tree | Leaf | Pharmaceutics aid, carminative |
| Phaya Yo | Cilacanthurus nutans (Burm. f.) Lindau | Acanthaceae | Scendent shrub | Leaf | Antiinflammatory, antiviral |
| Thian Khao | Cuminum cyminum f.) Lindau | Apiaceae | Herb | Fruit | Carminative, expectorant, antispasmodic |
| Khamin Chan | Curcuma longa L. | Zingiberaceae | Perennial herb | Dried rhizome | Stomachic, carminative, pharmacaceutics aid, astringent |
| Khamin Oi | Curcuma zedoaria (L.) Corrêa | Zingiberaceae | Perennial herb | Dried rhizome | Stomachic, antidiarrheal, emmenagogue |
| Lakiachan | Dracaena cochinchinensis (Lour.) S. C. Chen | Asparagaceae | Tree | Wood | Antipyretic, antinflammatory |
| Pla Lai Phueak | Eurycoma longifolia Jack | Simaroubaceae | Shrub | Roots | Antipyretic |
| Thian Khao Phueak | Foeniculum vulgare Mill. | Apiaceae | Herb | Dried cremocarp and mericarp | Carminative, spasmylytic |
| Krachai Daeng | Hibiscus sabdariffa L. | Malvaceae | Annual herb or subshrub | Dried persistent calyx and epicalyx | Diuretic |
| Maengjak Kha | Hyptis suaveolens (L.) Poit. | Lamiaceae | Subshrub | Dried aerial part | Carminative, antimicrobial (topical) |
| Krachai Dam | Kaempferia parviflora Wall. ex Baker. | Zingiberaceae | Herb | Rhizome | Tonic, carminative |
| Thian Daeng | Lepidium sativum L. | Brassicaceae | Annual herb | Seeds | Expectorant, stomachic |
| Kot Hua Bua | Ligusticum sinense Oliv. cv. Chuarxiong | Apiaceae | Herb | Dried Rhizome | Carminative, blood tonic for menstrual disorder |
| Bunnak   | Mesua ferrea L. | Calophyllaceae | Tree | Dried blooming flower | Cardiotonic, antipyretic |

(Continued)
| Thai name                        | Scientific name               | Family          | Habit                     | Parts used         | Treatment/application                                      |
|---------------------------------|-------------------------------|-----------------|---------------------------|--------------------|-----------------------------------------------------------|
| Phrikun (ขิง)                   | Mimulusops elengi L.          | Sapotaceae      | Tree                      | Dried flower       | Tonic, antipyretic                                        |
| Mara Kh K Nok (มะกรวย)         | Momordica charantia L.        | Cucurbitaceae   | Annual or perennial climber | Fruit             | Bitter tonic, internal heat alleviating                   |
| Mon (โมน)                       | Morus alba L.                 | Moraceae        | Deciduous tree or shrub   | Leaf               | Mild antiviscous                                          |
| Kot Chada Mangsi (กอตช่ามังสี)  | Nardostachys jatamansi (D. Don) DC. | Caprifoliaceae | Herb                      | Roots, Rhizome     | Mild sedative, treatment of dysmenorrhea                 |
| Bua Luang (บัวหลวง)            | Nelumbo nucifera Gaerthn.     | Nelumbonaceae   | Perennial herb             | Dried stamen       | Cardiotonic, antipyretic                                  |
| Kot Kan Phrao (คอกันพราว)      | Neopicrocrhis acrophiliana    | Plantaginaceae  | Perennial herb             | Rhizome            | Antipyretic, stomachic                                   |
| Thian Dam (ธิดี)                | Nigella sativa L.             | Ranunculaceae   | Annual herb                | Seed               | Carminative, diuretic                                    |
| Kaphrao Daeng (กําพะร้าว)       | Ocimum tenuiflorum L.         | Lamiaceae       | Herb                      | Dried leaf         | Pharmaceuticals aid, carminative                         |
| Ya Naat Maeo (ยานาทมาโอ)       | Orthosiphon aristatus (Blume) Miq. | Lamiaceae   | Perennial herb             | Dried leaf and stem tip | Diuretic                                                |
| Makham Pom (มะคัมปอม)          | Phyllanthus emblica L.        | Phyllanthaceae  | Small or medium sized tree | Dried mature fruit | Expectorant, laxative, antiscorbutic                     |
| Than Sattabut (ทันสตั้บ)         | Pimpinella anisum L.          | Apiceae         | Annual herb                | Dried ripe fruit   | Carminative, expectorant, pharmaceutic aid               |
| Phu (พุ)                        | Piper betle L.                | Piperaceae      | Woody climber              | Leaf               | Antiluful, antiallergic                                  |
| Phrik Thai Dam (พิชิตไทยدام)     | Piper nigrum L.               | Piperaceae      | Climber                    | fruit              | Aromatic, stomachic, carminative                         |
| Phrik Thai Lon (พิชิตไทยลอน)     | Piper nigrum L.               | Piperaceae      | Woody perennial climber    | Dried unripe fruit | Aromatic, stomachic, carminative                         |
| Di Pli (ดีปลี)                  | Piper retrofractum Vahl       | Piperaceae      | Woody climber              | Dried stem         | Carminative, stomachic, antinflammatory                  |
| Chaphlu (ช้างพลู)                | Piper sarmentosum Roxb.       | Piperaceae      | Herb                      | Leaf               | Carminative                                              |
| Sakhan (สะคัน)                 | Piper waliachi (Miq.)         | Piperaceae      | Woody climber              | Dried stem         | Carminative, stomachic, antinflammatory                  |
| Thian Klet Hoi (ท่านเกตฮอย)      | Plantago ovata Forssk.        | Plantaginaceae  | Herb                      | Seed               | Bulk-forming laxative                                    |
| Chan Daeng (ชันแดง)             | Pterocarpus santalinus L. f.  | Fabaceae        | Tree                      | Bark               | Antipyretic, antiinflammatory, cardiacitic               |
| Chan Khao (ชันขาว)               | Santalum album L.             | Santalaceae     | Tree                      | Dried heartwood    | Cardiotonic, stomachic, nerve tonic                      |
| Chumhet Thet (ชุมเห็ดเทศ)         | Senna alata (L.) Roxb.        | Fabaceae        | Herb or under shrub       | Dried mature seed  | Laxative, antiluful                                      |
| Chumhet Thai (ชุมเห็ดไทย)         | Senna tora (L.) Roxb.         | Fabaceae        | Herb or under shrub       | Dried mature seed  | Laxative, diuretic                                       |
| Mawaeng Khruea (มะแว่งเครือ)     | Solanum trifoliatum L.        | Solanaceae      | Slender scrambling shrub   | Fruit              | Expectorant                                              |
| Thaowan Piang (ต้าวันเพียง)       | Soleri scandens (Roxb.)       | Asteraceae      | Large woody Climber        | Dried stem         | Analgesic, antiinflammatory                              |
| Tanmon (ตานหม่อน)                | Socratis scabrida (DC.) H. Ade | Asteraceae      | Scabrida shrub             | Leaf               | Demulcent                                                |
| Samo Phiphek (สมอพิเภก)         | Tithonia diandra (Gaertn.)    | Combretaceae    | Large tree                 | Mature fruit       | Laxative, carminative, astringent, expectorant           |
| Samo Thai, Kot Phung Pla (สมอไทย  kot phlung pla) | Terminalia chebula Retz.     | Combretaceae    | Large tree                 | Mature fruit       | Laxative, carminative, astringent, expectorant           |
| Rangchuet (ระงขุ้ย)              | Thunbergia laurfolia Lindl.   | Acanthaceae     | Woody climber              | Leaf               | Detoxicant, antipyretic                                  |
| Boraphet (บอระเพ็ด)              | Tinospora crispa (L.) Hook. f. & Thom | Menispermacae  | Woody climber              | Dried stem         | Antipyretic, bitter tonic, stomachic                    |
| Thian Yaowaphani (ที่นัยวะพานี)  | Trachyspermum ammi (L.) Sprague | Apiaceae        | Annual herb                | Dried ripe fruit   | Carminative, pharmaceutic aid                           |
| Phrai (ปาก)                     | Zingiber montanum (J. König) Link, ex A. | Zingiberaceae | Herb                      | Dried rhizome      | Antiinflammatory, counterirritant, mosquito repellent |
| Khing (แข็ง)                    | Zingiber officinalis Roscoee | Zingiberaceae   | Perennial herb             | Dried rhizome      | Carminative, antiflulent                                |
| Krathue (กร้าธ)                  | Zingiber zenubet (L.) Sm.     | Zingiberaceae   | Herb                      | Dried rhizome      | Antiinflulental, stomachic                              |
TABLE 2 | Species admixtures in the herbal trade samples of medicinal plants listed in the Thai Herbal Pharmacopoeia and techniques employed for discrimination.

| Thai name          | Scientific name | Matrix type          | Total number samples | Percentage of species admixture detected | Declared/identified species | Discriminant technique employed | Reference                  |
|--------------------|-----------------|----------------------|----------------------|------------------------------------------|-----------------------------|---------------------------------|-----------------------------|
| Maksong (มาคสอง) | Areca catechu L. | Processed sample     | 45                   | 38.09                                     | Nil                         | Mini-DNA barcode                | Song et al., 2017            |
| Matum (แมตุม)    | Aegle marmelos, (L.) Correa | Leaf, root, fruit | 11                   | 0                                         | Nil                         | DNA barcode                     | Kumar et al., 2018           |
| Fa Thalai (สำเภา) | Andrographis paniculata (Burm.f.) Nees | Dried sample, powder, capsule, tea | 10                   | NQ                                        | Yellowish-green color of A. paniculata and A. cordifolia | DNA barcode | Osathanunkul et al., 2016 |
| Thian Ta Takkatan (เทียนตาตักทาน) | Anethum graveolens L. | N/A                   | N/A                   | NQ                                        | Trachyspermum ammi and Foeniculum vulgare | DNA barcode | Schori and Showalter, 2001 |
| Kot (โค้ท)         | Angelica dahurica (Hoffm.) Bert. & Hook. f. ex Franch. & Sav. | Root                  | 20                   | NQ                                        | A. anomala and A. japonica | DNA barcode and SCAR assay | Noh et al., 2018             |
| Kot Chiang (โค้ทชี้) | Angelica sinensis (Oklu.) Diels | Root                  | 13                   | NQ                                        | A. laxifolia and A. nitida | DNA barcode | Feng et al., 2010          |
| Kot Chiang (โค้ทชี้) | Angelica sinensis (Oklu.) Diels | Root                  | 13                   | NQ                                        | A. nitida | HPLC fingerprints | Lu et al., 2005 |
| Kot Chiang (โค้ทชี้) | Angelica sinensis (Oklu.) Diels | Root                  | 13                   | NQ                                        | A. nitida | HPLC fingerprints | Lu et al., 2005 |
| Phrik Khinu (พริกขี) | Capsicum annuum L. | Powder                | 5                    | NQ                                        | Beta vulgaris and Ziziphus nummularia | DNA barcode | Song et al., 2016          |
| Phrik Khinu (พริกขี) | Capsicum annuum L. | Powder                | 61                   | 14.75                                     | Garlic, spring onion, and/or onion | DNA barcode | Seethapathy et al., 2015 |
| Khun (ขุน)         | Cinnamomum zeylanicum L. | Powder, spice, tea    | 5                    | Nil                                       | Beta vulgaris and Ziziphus nummularia | DNA barcode | Seethapathy et al., 2015 |
| Thian Khao, Yira (เทียนขาวยา) | Curcuma longa L. | Dried and fresh plant tissue | 7                    | 58.54                                     | Nil | DNA barcode | Arunraj et al., 2016          |
| Khamin Chan (ขามิน) | Eurycoma longifolia Jack | Capsule, tablet, tea  | 46                   | 50 or more                                | Nil                         | DNA barcode and HPLC analysis | Abdubakar et al., 2018 |
| Pla Lai Phueak (ปลาไหลเผือก) | Eurycoma longifolia Jack | Capsule, beverage, instant coffee mix, tea | 11                   | 27                                        | Holoscolosum sp., Nigella arvensis, Nigella sativa, and Curcuma longa L. | DNA barcode and HPLC analysis | Fadzil et al., 2018 |
| Krachai Dam, Thai Ginseng (กระชายดำา) | Kaempferia parviflora Wall. ex Baker | Processed and packed commercial powder | 7                    | 58.54                                     | Nil                         | Bar-HRM analysis | Osathanunkul et al., 2017 |
| Bunnak (บุนนาค) | Mesua ferrea L. | Crude drug            | 6                    | 33                                        | Nil                         | DNA barcode | Kumar et al., 2018          |
| Thian Dam (เทียนดำา) | Nigella sativa L. | Seed                  | 10                   | NQ                                        | Allium cepa and Citronia guianensis | DNA barcode | Sudhir et al., 2016          |

(Continued)
mixtures of powdered CPMs for authentication, and other CPMs were generated through substitutions or as adulterants (Gao et al., 2017). Zhang et al. (2017) used SNPs for which traditional DNA barcoding has not been successful for the differentiation of Echinacea species.

Loop-mediated isothermal amplification (LAMP) is one of the approaches developed to identify herbal medicine species (Li et al., 2016). A study demonstrated that the recombinase polymerase amplification (RPA) assay can be developed into an efficient tool for the rapid on-site authentication of plant species in Ginkgo biloba herbal products to differentiate the two species G. biloba and Sophora japonica (as adulteration) (Liu et al., 2018). DNA barcoding and metabarcoding have potential for the quality control of herbal products (Raclariu et al., 2018). Recently, a study recounted the history of DNA-based methods for identification of botanicals, discussed some of the difficulties in defining a specific barcode or codes to use, and described how next generation sequencing technologies have enabled new techniques that can be used to identify these products with great authority and resolution (Moraes et al., 2015). High-throughput sequencing (HTS) methods were used effectively in the quality control and identification of food components. The HTS platforms, Illumina, and Ion Torrent, were used for the analysis of herbal teas, which yielded congruent results, both qualitatively and quantitatively (Speranskaya et al., 2018). These studies confirm that species admixtures may occur in the raw herbal trade. An intrinsic problem associated with the adulteration of herbal products is the effect it may have on user health and safety (Valiathan, 2006; Seethapathy et al., 2015; Srirama et al., 2017). Without regulation, such adulteration will decrease the efficacy and consumer confidence in herbal products, which will eventually cause economic damage to the raw herbal trade (Srirama et al., 2017).

TABLE 2 | Continued

| Thai name | Scientific name | Matrix type | Total number samples | Percentage of species admixture detected | Declared/identified species | Discriminant technique employed | Reference |
|-----------|----------------|-------------|----------------------|-----------------------------------------|-----------------------------|---------------------------------|-----------|
| Thian Dam (เทียนดำา) | Nigella sativa L. | Seed oil | N/A | NQ | Grape seed oil | Fourier transform infrared (FTIR) spectroscopy and gas chromatography | Nurrulhidayah et al., 2011 |
| Phrik Thai (พริกไทย) | Piper nigrum L. | Fruit | N/A | NQ | Carica papaya | HPLC and antioxidative assay markers | Menghani et al., 2010 |
| Phrik Thai (พริกไทย) | Piper nigrum L. | Powder | 9 | NQ | Chili | DNA barcode and HPLC RAPD markers | Parvathy et al., 2014 |
| Phrik Thai (พริกไทย) | Piper nigrum L. | Seed | N/A | NQ | Carica papaya | DNA barcode and HPLC RAPD markers | Khan et al., 2010 |
| Chan Khao (จันทน์ขาว) | Santalum album L. | Oil | 38 | NQ | Nil | Gas chromatography–mass spectrometry | Howes et al., 2004 |
| Chan Khao (จันทน์ขาว) | Santalum album L. | Oil | 6 | NQ | Nil | Multidimensional gas chromatography–mass spectrometry | Sciarrone et al., 2011 |
| Samo phiphek (สมอพิเภก) | Terminalia bālinica (Gaertn.) Roxb. | Fruit | 10 | 0 | Nil | DNA barcode | Kumar et al., 2018 |
| Samo phiphek (สมอพิเภก) | Terminalia bālinica (Gaertn.) Roxb. | Crude drug | 12 | NQ | Nil | PCR-RFLP and amplification refractory mutation system (ARMS) | Intharaksa et al., 2016 |
| Samo Thai (สมอไทย) | Terminalia chubula Retz. | Fruit | 13 | 0 | Nil | DNA barcode | Kumar et al., 2018 |
| Samo Thai (สมอไทย) | Terminalia chebula Retz. | Immature fruit | N/A | NQ | Nil | Chromatographic fingerprint analysis | Xie et al., 2006 |
| Rangchuet (ร่างจืด) | Thunbergia laurifolia Lindl. | Leaf | 8 | NQ | Nil | PCR-RFLP | Suwanchakasem et al., 2013 |
| Rangchuet (ร่างจืด) | Thunbergia laurifolia Lindl. | Both fresh and dried sample, powder | 10 | NQ | Nil | Bar-HRM analysis | Singleton and Osathanunkul, 2015 |

NQ, Not quantified; N/A, Not applicable.
Policies and Regulations Concerning Herbal Medicines

Recently, the large-scale international trade of herbal products has increased the concern for the safety and efficacy of herbal products (Walker and Applequist, 2012; Newmaster et al., 2013; Techen et al., 2014; Srirma et al., 2017). Since most herbal medicines are used in crude formulas in combinations of several herbs and often have extended usage, it is important that the species being used undergo strict validation, safety assessment, and quality and regulatory approval, similarly to modern medicinal drugs (Srirama et al., 2017). With continued development and improvements in DNA barcoding technology, especially with the combination of high-throughput techniques developed for DNA barcoding, a large number of samples can be assessed (Srirama et al., 2017). This technology could ensure the validation of raw herbal products and the identification of a large number of species via DNA-based methods (Srirama et al., 2017).

Although herbal medicines are widely used in healthcare systems for the treatment, diagnosis, and control of disease, quality control and proper regulation remain the foremost challenges worldwide. Every nation has its own official compendiums detailing the standardization and quality procedures for traditional medicine production. Although the WHO has passed stringent regulations related to traditional product production and formulation, very few countries have implemented regulations for herbal medicines, and most countries do not have proper guidelines for botanicals. Therefore, the quality of traded medicinal herbal products is not guaranteed (WHO, 2017).

Thailand became the 26th member of the WHO in 1984, which was a year after the Adverse Drug Reaction Monitoring Center (ADRMNC) was associated under the authority of the Thai Food and Drug Administration (Thai FDA) (WHO, 2017). The Thai FDA collects reports from health product surveillance systems and programs through a database, Thai herbal database. The Thai herbal database is a potentially effective data source for identifying adverse events related to herbal products (Saokaew et al., 2011). This database provides specific data with respect to the adverse status of a particular plant species (http://thaihvc.fda.moph.go.th/thaihvc/index.jsf#). However, there is an immediate need for a quality check portal before it reaches the consumer.

Quality Control: Centralized Testing Laboratory Proposition

Natural products are gaining popularity each day due to their safety and availability at an affordable price. The words “herbal,” “natural,” and “plant-derived” can be misleading at times, and it is important for the public to be made aware that herbal mixtures are medicines in their own right (Fan et al., 2012). Herbal medicinal preparations are formulations commonly consisting of 5 to 15 different herbs or a complex formulation consisting of several medicinal herbs and chemical drug constituents. A single herbal medicine can contain many natural constituents and/or a combination of numerous herbs that can give rise to interactions with hundreds of natural ingredients (Choi et al., 2002). This demands multiple stages of assessment of herbal extracts or products, such as pharmaceutical documentation, toxicology studies, and clinical studies for quality, safety, and efficacy, before entering the market.

A strong regulatory mechanism must be implemented to screen the safety, identity, and quality of herbal products (Srirama et al., 2017). Central to such a regulatory structure is the establishment of an effective entity to evaluate the credibility of species, assess the authenticity of the raw herbal products, and connect these data with trade regulators, both nationally and internationally. To safeguard the integrity of herbal trade, trade partners may need to access and utilize a biological reference guide developed through molecular diagnostic tools coupled with metabolite profiling. Ensuring herbal medicine quality also makes the products safer and more reliable, efficacious, sustainable, and marketable (Srirama et al., 2017). Imports and exports can be governed by such validations certified by nationally recognized government bodies/ agencies (Figure 1). It is important that such a governing body also sets up a regulatory system wherein both traditional medicinal plants and their herbal products are placed. Furthermore, it is important that the molecular tools (DNA sequences) and chemical metabolite profiles are also available along with the herbal plant samples (Srirama et al., 2017). These tools would provide a simple reference for validation. However, Thai medicinal products containing mixtures of numerous herbs make it difficult, time consuming, and expensive to meet the requirements of identification (both by DNA-based and metabolite-based methodologies). However, with the emergence of new technologies, especially next-generation and high-throughput techniques, a large number of samples can be evaluated through meta-barcoding and chemical analysis. In addition to the potential for frequent authentication of herbal products, this setup can also identify a wide variety of medicinal plant species.

Safe and stable herbal extracts may be marketed if their therapeutic use is well documented and certified by a CT laboratory. There is an urgent need to develop a digital key that would enable easy identification of medicinal plants and their products, which could integrate floristic details, trade, drug databases, and DNA barcoding information (Figure 2). Electronic access to such database information can be made possible with internet access and international data sharing efforts, where a wealth of chemical and DNA sequence information can be made available and samples be compared. Users can easily search and compare by plant name or drug name to obtain complete details.

Conclusions

Medicinal plants and their products are extensively used in the indigenous and modern healthcare systems in Thailand and many countries. The international trade of herbal products has a major impact on the international economy, and the demand for herbal products is growing in both
FIGURE 1 | Proposed regulatory framework of traded herbal drugs of Thailand.
developing and developed countries. This increase in demand has resulted in the substitution and adulteration of medicinal plants with other herbal products whose health benefits are unknown. The results of this study would potentially be useful in providing recommendations to address the increasing concerns of adulteration in raw drug trade and to propose mechanisms that can ensure quality standards in raw drug markets.

Our observations clearly support the claim that there is no established mechanism to connect and coordinate the herbal industry for the certification of herbal products in Thailand. Therefore, we propose the Thai herbal database that contains data on all medicinal plants, including floristic details such as taxonomic hierarchy, vernacular names in various languages, habitat, cultivation type, worldwide distribution maps, Thailand distribution maps (state and district), species images, herbarium images, general photographs, line diagrams, and synonyms. Genetic data include DNA marker information, gene sequences, GenBank accession number details, and chemical data include details of various kinds of tests such as TLC identity test, gas chromatography, gas liquid chromatography, and estimation of chemical compounds in drugs using HPLC and a complete list of major chemical constituents (marker compounds). It also contains a list of other chemical constituents and possibly important chemical compound structures as well as the status of import–export trade and the details of admixtures found in those particular plants. This database could play an important role in monitoring the medicinal plant trade and could be a promising initiative in Thailand for the development of science and technology and to provide consumers with access to all essential information. This herbal database concept could be a novel strategy in Thailand, generating transparency for all safety and quality measures and facilitating the prevention of admixtures in the herbal trade. This herbal database should be developed with utmost planning and made available to all researchers, academicians, people involved with regulatory policy and industry, and, most importantly, common people so that they may gain access to past and present studies. Additionally, in our opinion, accessibility of this herbal database to all researchers, traders, and consumers will allow the sensible development of drug safety measures. The use of this concept can allow governing bodies to improve the efficacy of herbal drugs at a considerable cost.

**AUTHOR CONTRIBUTIONS**

Conceptualization and design of the study: SS and SK. Data collection and formal analysis: SK. Validation and visualization: SK and CT. Conclusion: SS. Manuscript writing: SK. Review and editing: SS and SK.

**FUNDING**

The Ratchadaphisek Somphot Endowment Fund, Graduate School, Chulalongkorn University provided funding which was used to assist in the preparation of this review.
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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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