A Review of Traditional Uses, Phytochemistry and Pharmacological Properties of Some Vietnamese Wound-Healing Medicinal Plants

Oanh Hoang Hua¹, Quynh Thi Thuy Tran¹, Dieu-Thuong Thi Trinh¹, Van-Dan Nguyen¹, Duc Phan Nguyen Duong¹ and Triet Thanh Nguyen¹

Abstract

Wound healing is a sophisticated process that results in the repair of damaged tissues. Any impairment to this process can lead to non-healing (chronic) wounds. Since these can cause a massive burden on the healthcare system, alternative therapies that promote wound healing should be considered. Therapies of natural origins that are safe and with no adverse side effects are especially promising. Vietnam, a tropical-climate country, has many medicinal plants that possess the potential for healing wounds. This report explores the use of some common plants used in Traditional Vietnamese medicine and their molecular mechanisms.

Keywords

traditional vietnamese medicine, anti-bacterial, anti-inflammation, wound-healing, medicinal plants

Received: September 14th, 2021; Accepted: March 1st, 2022.

Introduction

Wound healing is a physiological process comprising the collaboration of many cell types and their products to respond to the injury of tissues.¹ Generally, the wound healing process is divided into four overlapped stages: haemostasis, inflammation, proliferation, and matrix remodeling.² Impairment at any stage of this well-orchestrated healing process can result in non-healing wounds. A non-healing wound is generally defined as one that will not heal within twelve weeks.² This chronic condition puts patients at a significant health risk for impaired mobility, limb amputation, or even death.³ To reduce the massive burden of non-healing wounds in the healthcare system, increased efforts are underway to explore alternative therapies that accelerate wound healing.⁴ Among them, natural wound healing products that have been used for thousands of years are receiving increased interest because of their efficacy and safety.⁵

Wound healing medicinal plants have been used from the beginning of Traditional Vietnamese Medicine (TVM) practices. These practices were recorded in “Nam Duệ thâm hưu” [Miraculous Medicines of the South] – one of the most ancient and famous TVM books written by Tự Thịnh (1330-e. 1389), who was a Buddhist monk and also the Ancestor of Traditional Vietnamese Pharmacy. Most of these natural drugs are common and easily found in many areas from the north to the south of Vietnam.⁶,⁷ Wound healing medicinal plants also played an important role in treating burns in the Vietnamese – American war (1965-1975).⁸ Since these traditional healing practices⁹ were largely transmitted verbally throughout the ages, many effective practices have been either lost or are now fading away.³ In addition, patients in Vietnam tend to self-medicate using both Western and herbal medicines.⁸ Furthermore, many practitioners, especially local healers, use self-collected plants according to their experience.⁸ These reasons are partly responsible for the lack of clinical evidence-based supporting traditional healing practices, leading to exaggerated drug efficacy claims that are out of proportion in TVM practices. This is in stark contrast to Western medicine, which coexists in the Vietnamese healthcare system.⁸

To provide an objective view about healing wound medicinal plants in Vietnam, in this review, we have summarized some of the common traditional herbal medicines used for healing wounds, the experience of using them in TVM, and some of their chemical components and the mechanisms that affect the process of wound healing.

¹Faculty of Traditional Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam
Corresponding Author:
Triet Thanh Nguyen, Faculty of Traditional Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, 221B Hoang Van Thu St, Ward 8, Phu Nhuan District, Ho Chi Minh City 72217, Vietnam.
Email: nguyenthanhtrie1702@ump.edu.vn

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access page (https://us.sagepub.com/en-us/nam/open-access-at-sage).
Some Medicinal Plants Used for Wound Healing in Traditional Vietnamese Medicine

Table 1 provides information about the chemical constituents of some medicinal plants and their activities that affect the wound healing process.

**Morinda citrifolia** L. (Rubiaceae) – Common Name: Noni

Chemical Constituents. The major chemical constituents that have been isolated from this plant are anthraquinones, flavonol glycosides, iridoid glycosides, lipid glycosides, and triterpenoids.

According to a book on Malaysian medicinal plants, various chemical constituents have been found in different parts of *M. citrifolia*, such as: 5,7-acacetin-7-O-β-D-(+)-glycopyranoside, ajmalicine isomers, alizarin, asperuloside, asperulosidic acid, chrysophanol, damacanthal, digoxin, 5,6-dihydroxyluclidin, 5,6-dihydroxyluclidin-3-β-primeveroside, 5,7-dimethylpygenin-4′-O-β-D-(+)-galactopyranoside, lucidin, lucidin-3-β-primeveroside, 2-methyl-35,6-trihydroxyanthraquinone, 3-hydroxymorindone, 3-hydroxymorindone-6-β-primerosereose, α-methoxylarzarin, 2-methyl-35,6-trihydroxyanthraquinone-6-β-primeveroside, mono-ethoxyrubiaedit, morindadiol, morindone (15,6-trihydroxy-2-methylnanthraquinone), morindone-6-β-primeverose, nornannacanthal, quinoline, rubiadin, rubiadin 1-methyl ether, saroniodi, ursoic acid, alkaloids, anthraquinones and their glycosides, caproic acid, caprylic acid, fatty acids and alcohols (C5-9), flavones glycosides, flavonoids, β-D-glucopyranosyl, indoles, purines, and β-sitosterol. We report herein some representative compounds in the medicinal parts being commonly used in Vietnam: Asperulosidic acid, asperuloside tetracetaet, 2,6-di-O-(β-D-glucopyranosyl-1-O-octanoyl)-β-D-glucopyranosyl, 6-O-(β-D-glucopyranosyl-1-O-octanoyl)-β-D-glucopyranosyl, caproic acid, caprylic acid, ethyl caprylate, ethyl caproate, hexanoic acid, octanoic acid, quercetin 3-O-α-L-rhamnopyanosyl-(1-6)-β-D-glucopyranoside (from fruit); morindone, damnacanthal, 8-hydroxy-8-methoxy-2-methylnanthraquinone, rubichloric acid, 1,3-dihydroxy-6-methyl anthraquinone, morone 1, morenone 2, ruberythric acid, and rubiadin (from root). The methanol extract of *M. citrifolia* fruit is rich in phenolic content, which was proven to be potent for antioxidant activity.

Till now, 51 volatile compounds have been identified in *M. citrifolia* ripe fruit, without clear specification of the fruit harvest locations and stage conditions. These compounds are organic acids (for example, octanoic acids, hexanoic acids), esters (for example, methyl octanoate, methyl decanoate), ketones, (E)-6-dodecenyl—lactone, or alcohols, including 3-methyl-3-buten-1-ol.

Mechanism. Noni leaf juice (the juice obtained by pressing M. citrifolia leaves mechanically) was found to bind to both PDGF and A2A receptors, with the affinity of the juice to the PDGF receptors being higher than that to the A2A receptors. The juice seemed to be an agonist of ligand binding on the PDGF receptors. Noni leaf juice and the leaf extracts (ethanol extract and its n-hexane and MeOH fractions) promote wound healing by increasing ligand binding at the A2A and PDGF receptors and also by increasing the wound closure rate as its mechanisms of action.
| Scientific name | Common name | Plant parts - Formulation | Chemical constituents | Mechanisms | References |
|---------------|-----------|--------------------------|-----------------------|------------|-----------|
| *Morinda citrifolia* L. | Noni | Leaves | Flavonoids | Anti-bacterial | Trieu et al. (2020) |
| | | | | Anti-inflammation | |
| | | | | Decrease wound size, promote tissue regeneration | |
| | | Fruits | Tannin, triterpenoids | Reduce the amount of dead tissue and enhance wound healing on streptozotocin-induced diabetic rats | Nayak et al. (2007) |
| *Morus alba* L. | White mulberry | Roots | Hydroxymoracin N, albanol A, kuwanon G, sanggenon isomer, kuwanon A, morusinol, mulberranol | Stimulates the expression of the genes and upregulated the mRNA level involved in keratin filament in mouse skin explant culture | Kim et al. (2015) |
| | | Leaves | Stilbenes, oxyresveratrol and resveratrol | Anti-oxidant | Nitish et al. (2014) |
| *Eclipta prostrata* L. | False daisy | Aerial parts, leaves | Steroids, alkaloids, triterpenoids | Anti-diabetic | Ampa et al. (2018), Arunachalam et al. (2009), Jahan et al. (2014) |
| | | | | Anti-inflammatory | |
| | | | | Absorb UVA and UVB irradiation | |
| *Centella asiatica* L. | Gotu kola | Aerial parts | Madecassoside, madecassic acid, asiaticoside, asiatic acid | Increase the speed and quality of wound healing | Hussain et al. (2019), Wu et al. (2012) |
| *Calophyllum inophyllum* L. | Tamanu | Seed oil | Callophyllolide, inophyllolide | Anti-inflammation, antifungal, antibacterial and insecticidal | Tropical Plants Database, Ken Fern (2021), Ansel et al. (2016), Nguyen et al. (2017) |
| *Momordica charantia* L. | Bitter melon | Aerial parts, Fruits | Polysaccharides, peptides and proteins, lipids, terpenoids, phenolics, sterols | Anti-bacterial | Hussan et al. (2014) |
| | | | | Anti-oxidant | |
| | | | | Anti-diabetes | |
| | | | | Enhance wound closure in diabetic rats | |
| *Kalanchoe pinnata* (Lam.) Pers. | Cathedral bells | Leaves | Flavonoid, steroidal glycosides | Promote re-epithelialization and denser collagen fibers | Zakharchenko et al. (2017), Coutinho et al. (2020), Nayak et al. (2010), Rajsekhar et al. (2016) |
| | | | | Antifungal | |
| | | | | Decrease wound size | |
| *Averrhoa carambola* L. | Star fruit | Fruits | Proanthocyanin, vitamin C, gallic acid | Anti-oxidant | Cabrini et al. (2011), Lakmal et al. (2021), Muthu et al. (2016) |
| | | | | Anti-inflammation | |
| | | | | Anti-bacterial | |
| | | | | Antifungal | |
| *Benincasa hispida* (Thunb.) Cogn. | Wax gourd | Fruits | Phenolic contents | Anti-oxidant | Lubna et al. (2013), Racheh et al. (2011), Park and Lee (2020) |
| | | | | Anti-inflammation | |
| | | | | Anti-bacterial | |
| | | | | Antifungal | |
| | | | | Skin whitening | |
| *Vigna angularis* (Willd.) Ohwi & H. Ohashi | Adzuki bean | Seeds | Flavonoid (Rutin) | Anti-oxidant | Hwang et al. (2014) |
| | | | | Prevent skin photoaging by UVB radiation | |
| | | | | Anti-inflammation | |
| *Hibiscus rosa-sinensis* L. | Chinese hibiscus | Flower, leaves | Flavonoid | Anti-bacterial | Jiang et al. (2015) |
| | | | | Immuneologic enhancement | |
| | | | | Anti-oxidant | |
| | | | | Androgen like Anticonvulsant | |
| | | | | Hypoglycemic | |
new compound, (2R,3R,4R)-2-hydroxymethyl3,4-dihydroxypyrrolidine-N-propionamide. Several bioactive compounds, including moracin Q, moracin T, artocarpesin, cycloartocarpesin, moracin R, moracin S, moracin U, moracin G, moracin, and kuwanon G were isolated from stem bark of *M. mesozygia*, another species of *Morus*. These compounds exhibited great antimicrobial potential against various species of microbe.13

**Mechanism.** Previous studies reported that *M. alba* root extract had multiple impacts on mouse skin explant culture: Enhanced outgrowth of epithelial cells and up-regulation of the mRNA level keratin filaments, stimulation of the expression of the genes involved in keratin filaments, and induced alteration of genes involved in the CXCL12/CXCR4 signaling pathway.12

A previous study suggested that a cream containing the aqueous extract of leaves of *M. alba* helped thermal burn wounds recover faster and reduced tissue damage in rats. This effect was attributed to the anti-oxidant activity of stilbenes, oxyresveratrol, and resveratrol in the leaf extract.13

*M. alba* leaf extract has long been used as a beneficial ingredient for skincare. It contains antioxidant properties, which help prevent the formation of wrinkles, and slow down the aging process.13

Resveratrol in *M. alba* is considered to be the main compound to protect the skin from being damaged by UV radiation and reduce melanin production. In addition, β-carotene, riboflavin (B2) compounds and vitamins A, C, and E contained in the extract help eliminate free radicals and prevent premature aging of the skin.13

**Eclipta prostrata** L. (Asteraceae) – Common Name: False Daisy

**Chemical Constituents.** Phytochemical analysis of *E. prostrata* aerial parts (stems, leaves and flowers) led to the isolation of ethyl-2,6-dihydroxy-4-methoxybenzoate, merulonic acid C, wedelolactone, dimethyl wedelolactone and quercetin. Several interested phenolic compounds have also been isolated from this plant, such as luteolin-7-O-β-D-glucoside, 3,4-dihydroxybenzoic acid ethyl ester, luteolin sulfate, apigenin sulfate, luteolin, wedelolactone, 7-0-methylorobol-4′-O-β-D-glucoside, apigenin, and 3′-hydroxybiochanin A.44,45

Further research led to the isolation and structural elucidation of a new isoflavonoid glycosides, 7-O-methylorobol-4′-O-β-D-glucopyranoside, together with seven known compounds, 3′-hydroxybiochanin A, echinocystic acid 28-O-β-D-glucopyranoside, eclipitasaponin A, eclabasaponin I, eclabasaponin IV, echinocystic acid, and 3-oxo-16α-hydroxyolean12-en-28-oic acid. For the first time, echinocystic acid-28-O-β-D-glucopyranoside was obtained from this genus.46

**Mechanism.** In traditional medicine, the leaves of *E. prostrata* have been used to treat diabetes and wounds. The antidiabetic and wound healing properties of this plant have been proven to be successful.14 It affects the proliferative phase and the epithelialization of the formation of granulation tissue process.47 Numerous compounds are responsible for the healing capacity of *E. prostrata*.48

In carrageenan and egg white induced hind paw edema in rats, oral administration of a 95% methanolic extract of leaves of *E. prostrata* at a dose of 100 mg/kg and 200 mg/kg showed a remarkable dose dependent anti-inflammatory activity.15

The *E. prostrata* extract was also found to absorb UVA and UVB irradiation. A dose-dependent protection was demonstrated of HaCaT human keratinocytes and mouse fibroblasts 3T3 cells against UVB-induced cytotoxicity. The protective effect against skin cell damage was attributed to a synergistic effect between chlorogenic acid and other active components present in the extract.16

**Centella asiatica** L. (Apiaceae) – Common Name: Gotu Kola

**Chemical Constituents.** Chong and Aziz49 reported that *Centella* leaves contain triterpenes which have been shown in animal studies to have anti-inflammatory and wound healing activities.

The triterpenes isolated from *C. asiatica* are the most frequent pentacyclic triterpenic acids comprising asiatic acid, asiaticoside, madecassic acid, madecassoside, brahmoside, brahmic acid, and brahminoside; other triterpene glycosides of *C. asiatica* are of the ursane- and oleanane-type.50 The most investigated compound of *C. asiatica* is asiaticoside.51 Other constituents reported for *C. asiatica* include essential oil, flavonoids, such as quercetin and kaempferol,50-52 and sterols, such as campessterol, sitosterol, and stigmasterol.51

**Mechanism.** Asiaticoside, madecassoside, asiatic acid, and madecassic acid are considered to be the principal constituents for treating skin conditions. Previous trials have confirmed their healing for conditions such as burns, wounds, cellulitis, leproptic infections, and skin ulcers.53

Wu et al18 reported that, in *vitro*, asiaticoside and madecassoside stimulated the synthesis of collagen type I and type III in primary human skin fibroblasts by activating the TGF-β/Smad signaling pathway. In *vivo*, these compounds enhanced the speed and quality of wound healing in mice. Furthermore, madecassoside was found to be more effective than asiaticoside (for procollagen type I and type III synthesis in *vitro*, for wound healing speed, and for wound healing pattern from the histological aspect, in *vitro*, correspondingly).18

Hossain et al17 reported that asiatic acid and madecassic acid showed anti-inflammatory and apoptotic effects, respectively, while asiaticoside and madecassoside stimulated collagen (I, II, III) synthesis, and new blood vessel formation that significantly helps to heal burn wounds.

In Vietnam, *Centella* sp. is used either as a powder of ground leaves or fresh juice to apply topically to scars (especially pitted
or sunken scars caused by skin conditions, such as acne and chickenpox) for wound healing.

*Calophyllum inophyllum* L. (Calophyllaceae) – Common Name: Tamanu

**Chemical Constituents.** In a review by Susanto et al. the major constituents of the plant include inophyline, canophyllol, canophylic acid, calophyllolide, inophyllolide, inophyllin A and B, calophyline, calophyllum C, and inophyllin A. The different parts of *C. inophyllum* contain various constituents, including xanthones, coumarins, chromanones (flavonoids, biflavonoids), triterpenoids, and steroids. Two coumarin-type components of *C. inophyllum* are calanolides A and B. The resinous compounds in tamanu oil, which are attributed to the healing activity of the oil, contain mostly secondary metabolites from neoflavonoids and pyranocoumarin derivatives.55

**Mechanism.** The oil possesses cica-trizing properties, and anti-inflammatory, antifungal, antibacterial and insecticidal activity. Clinical tests indicated that the oil may reduce old scars. The latex and pounded bark are applied externally on wounds and ulcers, and the resin is used to treat wounds and insect bites.19

According to the study of Ansel et al., tamanu oil emulsion accelerated wound closure in the scratched monolayer of keratinocyte and fibroblast cells, and this effect was faster than that of vitamin C-treated cells.20

In 2017, Nguyen et al. reported that calophyllolide isolated from *C. inophyllum* reduced fibrosis formation and effectively promoted wound closure through anti-inflammatory activity in a mice model. The mechanisms for this anti-inflammatory activity were attributed to the down-regulation of the pro-inflammatory cytokines (IL-1β, IL-6, TNF-α) and up-regulation of the anti-inflammatory cytokine (IL-10), reduction in MPO, and switching of macrophages to an M2 phenotype.21

In Vietnam, tamanu oil or latex (which is called “mu u”) is often topically applied to burns or scars to heal wounds or to treat acne.

*Momordica charantia* L. (Cucurbitaceae) – Common Name: Bitter Melon

**Chemical Constituents.** *M. charantia* contains cucurbitacins, polysaccharides, ascobic acid, triterpenoids, saponins, polypeptides, flavonoids, alkaloids, and sterols.66

The fruits of *M. charantia* have been found to contain numerous bioactive compounds including carbohydrates, proteins, and lipids.67,68

**Mechanism.** Diabetes causes multiple abnormalities such as impaired immune response, neovascularization, growth factor deficiencies and decreased synthesis of collagen. All these conditions delay wound healing.70 Treatment with *M. charantia* fruit ointment accelerates the wound closure speed by stimulating the expression of TGF-β in diabetic rats. Along with anti-diabetic properties (highly TGF-β expression), the plant is a potential alternative therapy for the treatment of diabetic wounds.22

According to Sharma et al., rats treated with *M. charantia* extract showed a remarkable reduction in wound size and epithelization time in an excision wound model.

In Vietnam and some other tropical countries, the leaf juice is applied externally to treat inflammation of the sole of the foot, scabies and itchy skin. A paste of the leaves is applied as a poultice on cuts and wounds. The leaves are used to make an antiseptic bath for children. The fruit is used externally for the treatment of chapped skin.66

*Kalanchoe pinnata* (Lam.) Pers. (Crassulaceae) – Common Name: Cathedral Bells

**Chemical Constituents.** This plant contains organic acids, flavonoids, bufadienolides, triterpenoids and some ubiquitous compounds. The leaves contain malic acid.72

In the crude extracts of leaves of *K. pinnata*, Pereira et al. identified flavonoids and organic acids, including quercetin-3-O-α-L-arabinopyranosyl-(1→2)-α-L-rhamnopyranoside, kaempferol-3-O-α-L-arabinopyranosyl-(1→2)-α-L-rhamnopyranosyl, quercitin, and *trans*-p-coumaryl glucaric acid.

Zakharchenko et al. reported that the constituents of *K. pinnata* comprised two phenolic glucosides (syringic acid β-D-glucopyranosyl ester and 4′-O-β-D-glucopyranosyl-coumaric acid), nine flavonoids (including kaempferol, quercetin, myricetin, acetin, and diosmetin glycosides, and flavonol glycosides, quercetin (3-O-α-L-arabinopyranosyl-(1→2)-α-L-rhamnopyranoside) and myricetin (3-O-α-L-arabinopyranosyl-(1→2)-α-L-rhamnopyranoside)). Four bufadienolides (bersaldegenin-1-acetate, bersaldegenin A, bersaldegenin-3-acetate, and bersaldegenin-13,5-orthoacetate) were also reported in the plant.74 In addition, *K. pinnata* possesses blood-agglutinating lectins with Mr 44–47 kDa containing ~1.5% carbohydrate.75 Of all the phytochemicals isolated from *K. pinnata*, bufadienolides like bryotoxin A, B, and C, which are very similar in structure and activity as two other cardiac glycosides, digoxin and digoxin, possess antibacterial, antitumor, cancer preventative and insecticidal actions.76,78

**Mechanism.** Coutinho et al. reported that creams containing *K. pinnata* leaf aqueous extract (6%) and its major flavonoid, quercetin 3-O-α-L-arabinopyranosyl-(1→2)-α-L-rhamnopyranoside (0.15%), both result in better re-epithelialization and denser collagen fibers after 15 days of topical use in a rat excision model. The results from this research suggest that using *K. pinnata* crude extract should be more profitable than the isolated compound because the crude extract is low-cost and ready for use.24
Zakharchenko et al. demonstrated, for the first time, that the aqueous extract of transgenic K. pinnata leaves, which contain the antimicrobial peptide cecropin P1 (CecP1), possesses activity against Candida albicans in vivo. However, this effect was attributed to a synergy between the fungicidal activity of CecP1 and wound healing, revascularization, and immunomodulating properties of the natural bioactive components of K. pinnata.

Rajsekhar et al. reported that the ethanolic extract of A. carambola showed a significant wound-healing activity by decreasing the size of the affected site, as well as reducing edema in the wounded area. Nayak et al. indicated that the presence of steroidal glycosides and phenolic antioxidants may attribute to this phenomenon.

In Vietnam and many countries, the fresh leaves of K. pinnata are pounded and then applied to burns and used as poultices on boils and ulcers, or are placed on the soles of the feet in order to stop haemorrhages. The leaves can be made pliable by being held over the fire, and then are applied as a treatment on wounds, bruises, and boils.

Averrhoa Carambola (Oxalidaceae) – Common Name: Star Fruit

Chemical Constituents. Star fruits are a good source of various minerals and vitamins, such as magnesium, potassium, and phosphorous, as well as β-carotene L-ascorbic acid (vitamin C) and gallic acid.

Phytochemical and pharmacological studies indicate that extracts of the leaves, fruits, and roots of star fruit contain saponins, flavonoids, alkaloids, and tannins.

Investigations characterizing the secondary metabolites of A. carambola have identified two O-glycosyl flavonoid components: quercetin-3-O-β-D-glucoside and rutin. Other compounds identified included: β-sitosterol, lupeol, anthraquinone glucosides, cyanidin-3-O-β-D-glucoside, cyanidin-3,5-O-β-D-diglucoside, β-amyrin, and C-glycoside flavones, such as apigenin-6-C-β-L-fucopyranoside and apigenin-6-C-(2"-O-α-L-rhamnopyranosyl)-β-L-fucopyranoside, apigenin6-C-(2"-O-β-L-rhamnopyranosyl)-β-D-glycopyranoside.

Ten undescribed dihydrochalcone C-glycosides, carambolasides R1–R3, S1, S2, T1–T3, 3-hydroxycarambolaside T1, and 3-hydroxydycarambolaside P were isolated, along with carambolasides I and P from the leaves of A. carambola.

Mechanism. Studies have shown that star fruits contain compounds possessing an anti-oxidative effect, removing toxins from the body and supporting the immune system to protect against cancer, reactive oxidative species damage, and lipoperoxidation.

Research findings of Cabrini et al. indicated that, in croton oil-induced ear edema mice, topical treatment with A. carambola extracts showed an anti-inflammatory property by reducing edema and inhibiting MPO activity. The extracts also showed anti-bacterial activity against Staphylococcus aureus, Klebsiella spp., Escherichia coli, Pseudomonas aeruginosa and Bacillus cereus.

Treating diseases with star fruit leaves has its origin in local folklore. Bathing with star fruit leaves is useful in treating several skin disorders, such as urticaria, dermatitis, and diaper rash.

Benincasa hispida (Thunb.) Cogn. (Cucurbitaceae) – Common Name: Wax Gourd

Chemical Constituents. Benincasa hispida fruits contain volatile oils, flavonoids, glycosides, polysaccharides, proteins, carotenes, vitamins, minerals, β-sitosterin, and uronic acid. Using thin-layer chromatography, four main sugars, galactose, glucose, xylose, and sorbose, have been found in B. hispida peels.

In B. hispida seeds, fatty acids accounted for 20.7% to 24.3% of total chemical constituents, with 75.4% of them being saturated fatty acids. Linoleic acid, accounting for 67.4% of total fatty acids, was the main fatty acid component in the seed extract. The seeds also contained 58.4% of total dietary fiber and 11.6% of crude protein.

Mechanism. In the rat model, both the light petroleum and methanol extracts of B. hispida fruit at a dose of 300 mg/kg induced dose-dependent inhibition of carrageenan-induced paw edema, histamine-induced paw edema, and cotton pellet-induced granuloma.

The seed oil of B. hispida demonstrated an antibacterial activity against Micrococcus luteus, Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pasteurella multocida and Pseudomonas aeruginosa.

A study in Korea, published in 2020, indicated that by inhibiting α-MSH, which is responsible for melanogenesis, and down-regulating the expression levels of MITF, TRP-1 and TRP-2, B. hispida seed extract possesses anti-oxidant, anti-inflammatory, and skin whitening activities.

According to traditional medicine, B. hispida has a sweet taste and cool properties, with the effect of clearing heat, diuretic, edema, and detoxification. B. hispida is very good for the skin, changing the moisture level, and blurring melasma, and dark spots caused by acne. It has been used to remove acne bran and blackheads.

Vigna angularis (Willd.) Ohwi & H. Ohashi (Fabaceae) – Common Name: Adzuki Bean

Chemical Constituents. Adzuki bean seeds contain water, amino acids, fatty acids, carbohydrates, dietary fiber, minerals, such as calcium, magnesium, phosphorus, ferrous, and zine, and, vitamins (vitamin A, thiamin, riboflavin, niacin, vitamin B6, folate, ascorbic acid). The major amino acids in the beans are tryptophan, lysine, methionine, phenylalanine, threonine, valine, leucine, and isoleucine. The principal fatty acids are linoleic acid and oleic acid.

Liu et al. reported that in addition to rutin, the flavonoid contents of adzuki bean include catechin, quercetin-
3-O-rutinoside, quercetin-3-O-glucoside, and vitexin-4′-O-glucoside. The saponin extract of adzuki bean contains azukisaponin IV, azukisaponin VI, azukisaponin V, azukisaponin II, azukisaponin I and azukisaponin III.86

**Mechanism.** Following Hwang et al,33 in vitro study showed that the hot-water extract of *V. angularis* (VAE) significantly reduced the production of MMP-1 in UVB-exposed normal human dermal fibroblast cells. In vivo study in UVB-irradiated hairless mice, by enhancing elastin, procollagen type I and TGF-β1 expression, VAE that was both topically and orally administrated inhibited wrinkle formation and skin thickness. VAE can be effective in preventing skin photoaging accelerated by UVB radiation.

Collantes et al reported that VAE inhibited the progress of atopic dermatitis (AD)-like skin lesions by regulating immune mediators and cells.87

According to traditional medicine, azuki beans have a sweet, sour taste, and have beneficial effects as a diuretic, to treat diarrhea, and for detoxification, and are often used to treat hydrocephalus, bloating, rheumatism, pain, boils, itching, cholera, and dysentery.

**Hibiscus rosa-sinensis** L. (Malvaceae) – Common Name: Chinese Hibiscus

**Chemical Constituents.** Phlobatannins, glycosides, saponins, flavonoids, and terpenoids, including vitamins such as thiamine, riboflavin and niacin, have been reported in the leaves, flowers, stems and roots of *H. rosa-sinensis*. **88**

Although quercetin exists in all parts of *H. rosa-sinensis*, there is a slight difference in contents between each part of the plant. The phenotype yellow flowers contain numerous flavones such as cyanidin-3,5-diglucoside, cyanidin-3-sophoroside-3,5-glucoside, quercetin-3,5-diglucoside, and quercetin-3,7-diglucoside. The root barks contain cyclopropenoids. The flowers, stems, and leaves contain small amounts of cyanin and cyanidin chlorides, and leaves contain β-sitosterol, teraxeryl acetate, and malvalic acids.88

**Mechanism.** Jiang et al34 studied the use of bud extract of *H. rosa-sinensis* to test skin healing and the mechanism of repairing efficacy in animal models. Using the boils and carbuncles model, the healing condition of all KM mice were observed. The extract of *H. rosa-sinensis* accelerated the recovery rate of skin boils and full-thickness loss. Compared to the ethyl acetate and chloroform extracts, the n-butanol extract showed the fastest rate of repairing wounds. This healing effect is attributed to the antibacterial and immunological enhancement activities of *H. rosa-sinensis*.34

In induced excision, incision, and dead space wounds in rats, treatment with the ethanol extract of *H. rosa-sinensis* significantly promoted the rate of wound contraction, the wound-breaking strength, the rate of epithelialization, and increased the weight and hydroxyproline content of the granulation tissue.89

According to TVM theories, hibiscus leaves are light in color, absorbent and neutral in nature. The leaves possess calming, sedative, anti-bacterial, anti-inflammation, and mild bleaching effect. It is commonly used in TVM to treat bloody stools caused by the inflammation of intestines and mucous membranes, lymphadenopathy, acne waves, scabies scar, dream crystal, and lower zone.

Fresh Hibiscus leaves and flowers are often used externally to treat boils, pyoderma, mastitis, and lymphadenitis.

**Discussion**

Tuệ Tinh said that Vietnamese bodies are more compatible with medicines derived from the tropical flora and fauna of Vietnam.90 In Nam Dương Thành Hưu, many folk medicines have been used for wound and burn healing, including red bean (*Vigna angularis*), sponge gourd (*Luffa aegyptica*), mulberry (*Morus alba*), and betel (*Piper betle*). With increased urbanization in Vietnam, only some select medicines are now more popular and available, especially in cities. This review highlights wound healing plants that are readily available in today’s Vietnamese gardens. These include gotu kola, tamarind, bitter melon, cathedral bells, and star fruit.

Many phytochemicals and herbs highlighted in this review show a high level of efficacy in wound management. In local culture, TVM is still being treated as an equal to modern science. It is inappropriate to label TVM as “old” in Vietnam. It is clear that “there are some illnesses that only our medicine can treat” (Tuệ Tinh).91

Wounds and burns on the skin are very common, encountered in all places by people of all ages. In order to achieve high efficiency in the treatment of wounds and burns, it is necessary to provide an accurate diagnosis, select appropriate drugs, implement effective treatment methods for each wound and burn, and manage each stage of the wound healing progression.

Treatment methods for wounds and burns include local and systemic treatment. Drugs for the treatment of skin diseases can be temporarily divided into: topical drugs, antipruritic drugs, anti-infection drugs, antifungals, immunosuppressive modulators, traditional medicine, light therapy and a group of drugs to improve health. Along with modern medicine, TVM also plays an important role in the treatment of wounds and skin burns. This review introduces some medicinal plants that have been used for over a thousand years. These plants are available and convenient for treating wounds and skin burns. These plants include: Gotu kola, bitter melon, tamarind, red bean, wax gourd, rose mallow, and star fruit. Various herbal constituents have proven wound-healing properties. As an example, tannins could promote wound healing through free radical removal, increasing the contraction of the affected area and increasing the formation of blood vessels and...
fibroblasts. Other active principles, such as triterpenes, alkaloids, and flavonoids, have proven to be effective in this process.

However, large randomized clinical trials are necessary to provide concrete evidence supporting the use of TVM in wound management.

Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval
Not applicable, because this article does not contain any studies with human or animal subjects.

Informed Consent
Not applicable, because this article does not contain any studies with human or animal subjects.

ORCID iDs
Dieu-Thuong Thi Trinh https://orcid.org/0000-0002-3886-3210
Duc Phan Nguyen Duong https://orcid.org/0000-0002-8143-3451
Triet Thanh Nguyen https://orcid.org/0000-0001-6710-2448

Trial Registration
Not applicable, because this article does not contain any clinical trials.

References
1. Shaw TJ, Martin P. Wound repair at a glance. J Cell Sci. 2009;122( Pt 18):3209-3213. doi:10.1242/jcs.031187
2. Wilkinson HN, Hardman MJ. Wound healing: cellular mechanisms and pathological outcomes. Open Biol. 2020;10(9):2000223. doi:10.1098/rsob.2000223
3. Sagha zadeh S, Rinoldi C, Schot M, et al. Drug delivery systems and materials for wound healing applications. Adv Drug Deliv Rev. 2018;127(2018):138-166. doi:10.1016/j.addr.2018.04.008
4. Kasuya A, Tokura Y. Attempts to accelerate wound healing. J Dermatol Sci. 2014;76(3):169-172. doi:10.1016/j.jdermsci.2014.11.001
5. Kotian S, Bhat K, Pui S, et al. The role of natural medicines on wound healing: a biomechanical, histological, biochemical and molecular study. Ethiop J Health Sci. 2018;28(6):759-770. doi:10.4314/ejhs.v28i6.11
6. Lê Trần Đức. Tự Tính toán tap. Tài bản lần thứ 5. Nhà xuất bản Y học. 2007.
7. Adoriso S, Fierabracci A, Rossetto A, et al. Integration of traditional and western medicine in Vietnamese populations: a review of health perceptions and therapies. Nat Prod Commun. 2016;11(9):1409-1416. doi:10.1177/1934578X1601100949
8. Woerdenberg HJ, Nguyen TM, Vu DV, et al. Vietnamese Traditional medicine from a pharmacist’s perspective. Expert Rev Clin Pharmacol. 2012;5(4):459-477. doi:10.1586/ecp.12.34
9. Nguyen XMA, Bun SS, Olivi er E, Dang TPT. Ethnobotanical study of medicinal plants used by K’Ho-cil people for treatment of diarrhea in Lam Dong Province, Vietnam. J Herb Med. 2020;19(2019):100320-100361. doi:10.1016/j.jhermed.2019.100320
10. Trieu HL, Trang NMP, Oanh TKN, Quyen TBP, Xu K, Minh VL. Phytochemical analysis and wound-healing activity of noni (Morinda citrifolia) leaf extract. J Herbs Spices Med Plants. 2020;26(4):379-393. doi:10.1080/10496475.2020.1748159
11. Nayak BS, Isitor GN, Maxwell A, Bhogadi V, Ramdhall DD. Wound-healing activity of Morinda citrifolia fruit juice on diabetes-induced rats. J Wound Care. 2007;16(2):83-86. doi:10.12968/jowc.2007.16.2.27006
12. Kim KH, Chung WS, Kim Y, et al. Transcriptomic analysis reveals wound healing of Morus alba root extract by up-regulating keratin filament and CXCL12/CXCR4 signaling. Phytother Res. 2015;29(8):1251-1258. doi:10.1002/ptr.5375
13. Nitish B, Arunpreet S, Rohit S, et al. Evaluation of burn wound healing potential of aqueous extract of Morus alba based cream in rats. Vet World. 2014;3(6):378-383. Accessed August 7, 2021. http://www.phytopharmajournal.com/Vol3_Issue6_01.pdf
14. Aampa R, Morabandza CJ, Samba MCR, Elion IDGR, Diatewa M, Abena AA. Antidiabetic and wounds healing activities of Eclipta prostrata (asteraceae) leaves. Int J Adv Res (Indore). 2018;6(12):393-398. doi:10.21474/IJAR01/8151
15. Arunachalam G, Subramanian N, Pazhani GP, Ravichandran V. Anti-inflammatory activity of methanolic extract of Eclipta prostrata L. (Asteraceae). Afr J Pharm Pharm Sci. 2009;3(3):97-100. Accessed August 7, 2021. https://academicjournals.org/article/article1380874140_Arunachalam%20%20.pdf
16. Jahan R, Al-Nahain A, Majumder S, Rahmatullah M. Ethnopharmacological significance of Eclipta alba (L) hassk. (Asteraceae). Int Sch Res Notices. 2014;2014(2014):385969. doi:10.1155/2014/385969
17. Hossain MI, Rahman MA, Siddika A, et al. Burn and wound healing using radiation sterilized human amniotic membrane and Centella asiatica derived gel: a review. Regen Eng Transl Med. 2019;6(3):347-357. doi:10.1007/s40883-019-00122-5
18. Wu F, Bian D, Xia Y, et al. Identification of major active ingredients responsible for burn wound healing of Centella asiatica herbs. Evid Based Complement Alternat Med. 2012;2012(2012):848093. doi:10.1155/2012/848093
19. Tropical Plants Database, Ken Fern. Calophyllum inophyllum. tropical.theferns.info. Updated July 30, 2021. Accessed August 7, 2021. http://tropical.theferns.info/viewtropical.php?id=Calophyllum+inophyllum
20. Ansel JL, Lupo E, Mijouin L, et al. Biological activity of polynesian Calophyllum inophyllum oil extract on human skin cells. Planta Med. 2016;82(11–12):961-966. doi:10.1055/s-0042-108205
21. Nguyen VI, Truong CT, Nguyen BCQ, et al. Anti-inflammatory and wound healing activities of calophyllolide isolated from
22. Hassan F, Teoh SL, Muhamad N, Mazlan M, Latiff AA. Monomorica obtusa ointment synergize with fungicide activity of biogenic peptide cercepin P1. J Immunol Res. 2017;2017(2017):3940743. doi:10.1155/2017/3940743

23. Zakharchenko NS, Belous AS, Biryukova YK, et al. Immunomodulating and revascularizing activity of Kalanchoe pinnata variegata with fungicidal activity of biogenic peptide cercepin P1. J Immunol Res. 2017;2017(2017):3940743. doi:10.1155/2017/3940743

24. Coutinho MAS, Casanova LM, Nascimento L, et al. Wound healing cream formulated with Kalanchoe pinnata major flavonoid is as effective as the aqueous leaf extract cream in a rat model of excisional wound. Nat Prod Res. 2020;35(24):1-6. doi:10.1080/14786419.2020.1817012

25. Nayak BS, Marshall JR, Isitgor O. Wound healing potential of ethanolic extract of Kalanchoe pinnata lam. Leaf—a preliminary study. Indian J Exp Biol. 2010;48(6):572-576. Accessed August 14, 2021. http://nopr.niscar.res.in/bitstream/123456789/9083/1/IJEB%2048%286%29%20572-576.pdf

26. Rajsekhar PB, Bharani ARS, Ramachandran M, Angel JK, Rajsekhar SPV. The “wonder plant” Kalanchoe pinnata (linn.) pers.: a review. J Appl Pharm Sci. 2016;6(3):151-158. doi:10.7324/JAPS.2016.60326

27. Cahbati DA, Moresco HH, Imazu P, et al. Analysis of the potential topical anti-inflammatory activity of Averrhoa carambola L. In mice. Evid Based Complement Alternat Med. 2011;2011(2011):908059. doi:10.1093/ecam/neq026

28. Lakmal K, Yasawaradene P, Jayarajah U, Seneviratne SL. Nutritional and medicinal properties of star fruit (Averrhoa carambola): a review. Food Sci Nutr. 2021;9(3):1810-1823. doi:10.1002/fsn3.2135

29. Muthu N, Lee SY, Phua KK, Bhole SJ. Nutritional, medicinal and toxicological attributes of star-fruits (Averrhoa carambola L): a review. Bioinformation. 2016;12(12):420-424. doi:10.6026/97230630012420

30. Lubna T, Benazir C, Salma R. Antibacterial studies on Benincasa hispida and Nigella sativa oil. Int Res J Pharm. 2013;4(4):121-122. doi:10.7897/2303-8407.04422

31. Rachchh MA, Yadav PN, Gokani R, Jain SM. Anti-inflammatory activity of Benincasa hispida fruit. Int J Pharma Bio Sci. 2011;2(3):98-106. Accessed August 12, 2021. https://ijpbs.net/abstract.php?article=ODM3

32. Park GR, Lee JA. Anti-oxidant, anti-inflammatory and whitening effect of Benincasa hispida seed extract. Int J Adv Comput Technol. 2020;10(7):249-256. Accessed August 12, 2021. https://www.korescience.or.kr/article/JAKO2020201647074088.page

33. Hwang E, Park SY, Lee HJ, et al. Vigna angularis water extracts protect against ultraviolet B-exposed skin aging in vitro and in vivo. J Med Food. 2014;17(12):1339-1349. doi:10.1089/jmf.2013.3017

34. Jiang JY, Xu H, Bui XT, et al. Research in skin healing and repair function and mechanism of Hibiscus rosa-sinensis linn bud extract. Chin Pharm Bull. 2015;31(8):1085-1091. doi: 10.3960/j.issn.1001-1978.2015.08.012

35. Krishnaiah D, Nithyanandam R, Sarbatly R. Chapter 22: phytochemical constituents and activities of morinda citrifolia L. In: Venketeshwar R, ed. Phytochemistry — A Global Perspective of Their Role in Nutrition and Health. IntTechOpen; 2012:127-150. Accessed November 1, 2021. https://www.intechopen.com/chapters/32941.

36. Krishnaiah D, Bono A, Sarbatly R, Anisuzzaman SM. Antioxidant activity and total phenolic content of an isolated Morinda citrifolia L. Methanolic extract from poly-ethersulphone (PES) membrane separator. J King Saud University – Eng Sci. 2015;27(1):63-67. doi:10.1016/j.jsues.2013.01.002

37. Farine J-P, Legal L, Moretoux B, Le Quere J-L. Volatile components of ripe fruits of Morinda citrifolia and their effects on Drosophila. Phytochemistry. 1996;41(2):433-438. doi:10.1016/0031-9422(95)04556-6

38. Palu A, Su C, Zhou BN, West B, Jensen J. Wound healing effects of noni (Morinda citrifolia L) leaves: a mechanism involving its PDGF/A2A receptor ligand binding and promotion of wound closure. Phytother Res. 2010;24(10):1437-1441. doi:10.1002/ptr.3150

39. Almeida-Souza F, Cardoso Fde O, Souza BV, et al. Morinda citrifolia linn. Reduces parasite load and modulates cytokines and extracellular matrix proteins in C57BL/6 mice infected with Leishmania (Leishmania) amazonensis. PLoS Negl Trop Dis. 2011(10);8:1004900. doi:10.1371/journal.pntd.0004900

40. El-Beshbishy HA, Singab AN, Sinkkonen J, Pihlaja K. Hypolipidemic and antioxidant effects of Morus alba L. (Egyptian mulberry) root bark fractions supplementation in cholesterol-fed rats. Life Sci. 2006;78(23):2724-2733. doi:10.1016/j.lfs.2005.10.010

41. Kusano G, Orihara S, Tsukamoto D, et al. Five new nortropane alkaloids and six new amino acids from the fruit of Morus alba LINNE growing in Turkey. Chem Pharm Bull. (Tokyo). 2002;50(2):185-192. doi:10.1248/cpb.50.185

42. Asano N, Yamashita T, Yasuda K, et al. Polyhydroxylated alkaloids isolated from mulberry trees (Morus alba L.) and silkworms (Bombyx mori L.). J Agric Food Chem. 2001;49(9):4208-4213. doi:10.1021/jf010567e

43. Kuete V, Fozing DC, Kapche WF, et al. Antimicrobial activity of the methanolic extract and compounds from Morus alba LINNE growing in Turkey. Chin Pharm Bull. 2009;17(1):1-7. doi:10.1515/jcpm-2019-0026

44. Han LF, Zhao J, Zhang Y, Kojo A, Liu EW, Wang T. Chemical constituents from dried aerial parts of Eclipta prostrata. Chin Herb Med. 2013;5(4):313-316. doi:10.1016/s1674-6384(13)60047-7

45. Bensegueni A. Traditional ointments in the treatment of wounds and burns. University of Mentouri; 2007.
76. McKenzie RA, Franke FP, Dunster PJ. The toxicity to cattle and bufadienolide content of six Bryophyllum species. *Aust Vet J*. 1987;64(10):298-301. doi:10.1111/j.1751-0813.1987.tb07330.x

77. Yamagishi T, Haruna M, Yan XZ, Chang JJ, Lee KH. Antitumor agents, 110, bryophyllin B, A novel potent cytotoxic bufadienolide from *Bryophyllum pinnatum*. *J Nat Prod*. 1989;52(5):1071-1079. doi:10.1021/np50065a025

78. Rastogi RP, Mehrotra BN, eds. *Compendium of Indian Medicinal Plants*. Vol. 5. Central Drug Research Institute and Publications & Information Directorate; 1995.

79. Moreesco HH, Queiroz GS, Pizzolatti MG, Brighente IMC. Chemical constituents and evaluation of the toxic and antioxidant activities of *Averrhoa carambola* leaves. *Rev Bras Farmacogn*. 2012;22(2):319-324. doi:10.1590/s0102-695x2011005000217

80. Yang Y, Jia X, Xie H, Wei X. Dihydrochalcone C-glycosides from *Averrhoa carambola* leaves. *Phytochemistry*. 2020;174(2020):112364. doi:10.1016/j.phytochem.2020.112364

81. Al-Snafi A. The pharmacological importance of *Benincasa hispida*. A review. *Int J Pharm Sci Res*. 2013;4(12):165-170. Accessed August 12, 2021. http://www.ciplr.info/docs/IJPSR13-04-12-007.pdf

82. Chidan Kumar CS, Mythily R, Chandraju S. Extraction and mass characterization of sugars from ash gourd peels (*Benincasa hispida*). *Rasayan J Chem*. 2012;5(3):280-285. Accessed August 12, 2021. https://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.1064.5600&rep=rep1&type=pdf

83. Mandana B, Russly AR, Farah S, Noranizan M, Zaidul I, Ali G. Antioxidant activity of winter melon (*Benincasa hispida*) seeds using conventional soxhlet extraction technique. *Int Food Res J*. 2012;19(1):229-234. Accessed August 12, 2021. http://www.ifrj.upm.edu.my/19%20(01)%202011/(30)IFRJ-2011-161%20Mandana.pdf

84. Sew CC, Zaini NAM, Anwar F, Hamid AA, Saari N. Nutritional composition and oil fatty acids of kurund (*Benincasa hispida* (thunb.) cogn.] seed. *Pak J Bot*. 2010;42(5):3247-3255. Accessed August 16, 2021. http://www.pakbs.org/pjbot/PDFs/42(5)/PJB42(5)3247.pdf

85. Brink M, Belay G. *Plant resources of tropical Africa 1. Cereals and pulses*. PROTA Foundation; 2006.

86. Liu R, Cai Z, Xu B. Characterization and quantification of flavonoids and saponins in adzuki bean (*Vigna angularis* L.) by HPLC-DAD-ESI-MS(n) analysis. *Chem Cent J*. 2017;11(1):93-109. doi:10.1186/s13065-017-0317-x

87. Collantes TM, Rho MC, Kwon HJ, et al. Azuki bean (*Vigna angularis*) extract inhibits the development of experimentally induced atopic dermatitis-like skin lesions in NC/Nga mice. *Food Chem*. 2012;132(3):1269-1275. doi:10.1016/j.foodchem.2011.11.100

88. Missoum A. An update review on *Hibiscus rosa-sinensis* phytochemistry and medicinal uses. *J Ayu Herb Med*. 2018;4(3):135-146. Accessed August 15, 2021. http://www.ayurvedjournal.com/JAHM_201843_08.pdf

89. Nayak BS, Raju SS, Orette FA. Effects of *Hibiscus rosa-sinensis* L. (Malvaceae) on wound healing activity: a preclinical study in a Sprague Dawley rat. *Int J Low Extrem Wounds*. 2007;6(2):76-81. doi:10.1177/1534734607302840

90. Hoang BC. The revival and development of Vietnamese traditional medicine: towards keeping the nation in good health. In: Laurence MTC, Wahlberg A, ed. *Southern Medicine for Southern People: Vietnamese Medicine in the Making*. Cambridge Scholars Publishing; 2012:133-151.

91. Wahlberg A. Herbs, laboratories, and revolution: on the making of a national medicine in Vietnam. *East Asian Sci Technol Soc*. 2014;8(1):43-56. doi:10.1215/18752160-2406625