Supporting Information

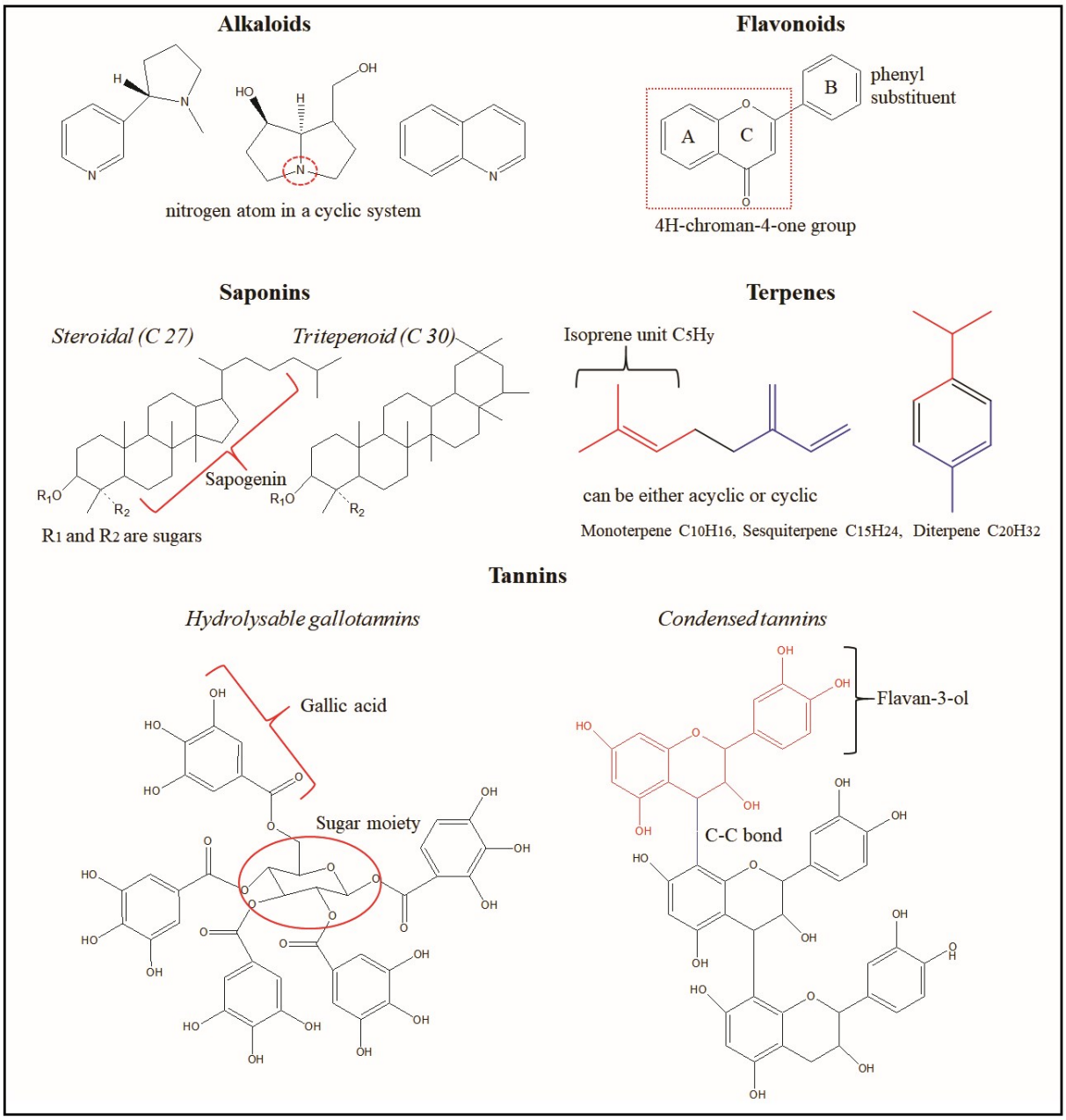

Figure S1. General chemical structure of the natural products families for wound healing

Table S1. Source, extraction and physico-chemical properties of alkaloids, flavonoids, saponins, tannins and essential oils

Natural product Family	Sources	Common extraction methods	Physico-chemical properties
Alkaloids [1]	Flowering plants (e.g. *Papaver somniferum, Alstonia Boonei, Croton lechleri*) Also present in some frogs and lizards	Solvent extraction using ethanol Silica gel chromatography Purification and identification can be done with HPLC	Contain nitrogen atoms in some cyclic system, leading to their alkalinity Usually colorless, odorless solids with a bitter taste
Flavonoids [2]	Present in several fruits and vegetables, roots, flowers, grains and tea.	Solvent extraction. Soxhlet apparatus using hexane for defatting, followed by ethyl acetate or ethanol.	Polyphenolic structure. Structure generally consists of a 15-carbon backbone with 2 phenyl rings and a heterocyclic ring with an embedded oxygen. Classified depending on the degree of oxidation, unsaturation of the linking chain and chemical structure. Often responsible for flower color.
Saponins [3]	Ginseng, Indian pennywort, soapwort, legumes such as kidney beans and lentils.	Solvent extraction using alcohols such as ethanol and methanol. Can be further purified using HPLC.	They are glycosides attached to a triterpene of steroid. Can be used as an emulsifying agent. Soluble in both water and fat. Bitter taste.
Tannins [4]	Various trees and shrubs such as black mimosa bark, oak bark, chestnut wood and mangrove wood, teas shrubs	Solvent extraction in water, alcohols or water. A Soxhlet apparatus can also be used. Purification and identification can be done using HPLC	Can broadly be classified as hydrolysable and condensed tannins. Molecular weights ranging from 500 to 20,000 Daltons. Possess an astringent taste and are soluble in polar solvents such as water and some alcohols.
Essential Oils [5]	Aromatic medicinal plants such as lavender, thyme, peppermint, tea tree. Fruit peels (e.g., citrus, orange) also used. Most commonly extracted from the flowers, leaves and bark.	Hydro-distillation, steam distillation or supercritical CO_2 extraction. Solvent extraction with non-polar solvents such as hexane can also be used.	Usually clear volatile oils with a pleasant smell. Often used for aromatherapy. Mixture of several compounds. Some pure essential oils can cause contact dermatitis

Table S2. *In vivo* results of alkaloids in wound healing

Molecule	Source	Wound healing models	Dosage	Wound healing phase	Action
Total alkaloid extract[6]	Root bark of *Alstonia boonei*	Sprague-Dawley rats of either sex	10 mg/ml and above	Proliferative	Anti-bacterial activity against several gram-positive and gram-negative strains. Faster re-epithelization than negative control and silver sulfadiazine treated groups.
Taspine [7,8]	Latex of *Croton lechleri*	☐Male Sprague-Dawley rats Full thickness paired linear incisions	250 µg	Proliferative	Non-toxic to human foreskin fibroblasts at concentration below 150ng/ml. Promote migration of fibroblasts in early phases of wound healing.
Betaine/ Betaine enriched ointment extract [9]	Pure compound from natural Remedies, India Plant extract from *Evolvus alsinoides*	☐Excision wound Inbred Wistar albino rats of either sex (6–7 weeks)	0.1380-0.3056 µg	Proliferative	Accelerate wound closure. Enhance collagenization due to chemotactic properties on fibroblast. Promote neovascularization.
Mahanimbicine [10]	Extract of *Murraya koenigii* compared to pure compounds	Full thickness wound Female Sprague Dawley rats	Thin layer of ointment containing 50 mg of molecule or extract applied twice daily for 14 days	Proliferative	Accelerate wound closure. Reduce infiltration of inflammatory cells. Promote fibroblast proliferation and enhance collagenization.

Table S3. *In vivo* results of flavonoids and saponins in wound healing

Molecule	Source	Wound healing models	Dosage	Wound healing phase	Action
Flavonoids					
Quercetin [11]	Sigma-Aldrich	☐Pressure ulcer model C57BL/6 mice	1 µM	Inflammatory	Accelerate wound closure. Anti-inflammatory- reduction in myeloperoxidase (MPO) + neutrophils, CD38+ macrophages, TNF-β, IL-1ß cytokines in wound area. Suppress activation of MAPK kinases-ENK, JNK and p38.
Quercetin [12]	Not provided	☐Diabetic wound Male Sprague-Dawley (SD) rats	10 - 40 mg/ml	Inflammatory	Accelerate wound closure in a dose dependent manner- better fibroblast and collagen distribution and angiogenesis rate- high expression level of CD31 and VEGF. Anti-inflammatory – Promote M1 to M2 polarization (low expression of ☐M1 marker iNOS and high expression of ☐M2 markers Msr-)1; low level of pro-inflammatory factors IL-6, TNF-α and high level of anti-inflammatory IL-10.
Quercetin [13]	Not provided	☐Full thickness wound Adult male Wistar rats	0.1 – 10%	Inflammatory	Accelerate wound closure at 0.1% quercetin-high fibroblast proliferation, thick and well-oriented collagen fibers. Antioxidant- No significant differences in levels of SOD, MDA, O_2 radicals, total thiols and proteins except for catalase. Increase in catalase in quercetin treated wounds.
Quercetin [14]	Not provided	Excision wound Wild-type C57Bl/6J mice	100 µL of 10 µM daily	Proliferative	Reduce scarring via fibrosis reduction resulting from an increase in cell surface expression of alpha-V integrin which promotes cell migration to the wound site in absence of excessive extracellular matrix deposition.

Luteolin (LUT)/ Flavonoids extract [15]	*Martynia annua Linn*. leaves (MAF)	☐Excision wound Wistar albino rats	0.2 - 0.5 % w/w	Remodeling	Accelerate wound closure and higher level of hydroxyproline - 100% and 87.61% closure; 51.67 and 39.62 mg/g for MAF and 0.5% LUT respectively compared to control (72.17% and 23.29%). No scarring and dense fibrous tissue and blood capillaries in MAF treated groups Antioxidant – Increase in SOD, CAT and GSH in 0.5% w/w LUT and MAF treated wounds.
Apigenin/ Crude extract of ☐flowers and their solvent or column fractions [16]	Flowers of *Helichrysum graveolens* (Hg)	☐Male Sprague–Dawley rats and Swiss albino mice Linear incision and circular excision wound model	1%	Inflammatory and remodeling	Apigenin, ☐Hg–MeOH, Hg–EtOAc, Hg–Fr.B accelerate wound closure with denser collagen deposition. Anti-inflammatory - Apigenin, Hg–MeOH, Hg–EtOAc, Hg–Fr.B inhibit inflammation by 27.8%, 37.1%, 30.7% and 24.5%. Antioxidant- Apigenin showed higher DPPH scavenging activity (IC_{50} -31.04 μg/ml) compared to quercetin (reference) (IC_{50}- 2.14 μg/ml).
Kaempferol (KM) [17]	Sigma-Aldrich	☐Male Wistar rats (3-4 months) Diabetic and non-diabetic Excision and incision wounds	0.5-1%	Inflammatory and remodeling	Accelerate wound healing in all conditions; promote hydroxyproline content to a larger extent in non-diabetic wounds than in diabetic wounds. General decrease in angiogenesis in both diabetic and non-diabetic rats. Tensile strength of wounds treated with 0.5% KM higher than those treated with 1% KM on day 14 in both conditions. Anti-inflammatory and antioxidant.
Naringenin [18]	Not provided	☐Hypertrophic scar model Female KM mice, 8-weeks-old	25-50 μM	Inflammatory and remodeling	Reduction in scar formation in dose dependent manner – decrease in α-SMA expression and number of α-SMA positive cells in naringenin treated wounds. Anti-inflammatory- Reduction in CD68+ cells and CD4+ cells in the scar tissues of a naringenin-treated mouse with dose dependency.
Genistein [19]	Sigma-Aldrich	Hypertrophic Scar	25-100 mmol/l	Remodeling	Scar reduction in dose and timely manner- reduced

		explant- ☐scar resection at 6– 12 months after severe burn. ☐Males & females people aged 10–37 years	added to culture media		stretching and proliferation of hypertrophic scar fibroblasts (HFSBs) (at 48 and 72h of culture only); reduced expression of COL I and COL III with 50 and 100 nmol/l of genistein. Suppress TPK activation and RTK-Ras- MAPK (ERK/p38) signal transduction in HSFBs. No significant effect on proliferation of normal human fibroblast *in vitro.*
Hesperidin [20]	Not provided	Diabetic and non-diabetic adult rats	10-80 mg/kg	Antioxidant, anti-inflammatory & angiogenesis	Dose-dependent increase in SOD, GSH and HDP activity and dose-dependent decrease in MDA and MPO, TNF-α and IL-6 levels. Maximum expression of VEGF in rats treated with 80mg/kg of hesperidin. Dose-dependent increase in VEGFR1 and VEGFR2 expression.
Formononetin [21]	Not provided	Transgenic Zebrafish models	25-50 µM	Proliferative & remodeling	Increase in angiogenic sprouting in subintestinal vessels (SIVs) in a dose dependent manner- 50 µM formononetin increased length of sprouting vessels and endothelial cell proliferation similar to the effects induced by VEGF-A injection.
Saponins					
Total ginseng saponins (Rb1, Rb2, Rc, Rd, Re, Rf, Rg1, Rg2, Rg3, Rh1 and Rh2) [22]	Korea Ginseng	ICR mice- incised skin wound		Inflammatory & proliferative	Accelerate re-epithelization by increasing rate of keratin cell migration; inhibit inflammatory reactions during early stage and promote collagen synthesis.
Ginsenoside Rb1 [23]	Red Ginseng roots	Male Balb/c mice (5 weeks old)- burn wounds	100 fg/ml-1 ng/ml	Proliferative	Enhance neovascularization *in vitro* by increasing VEGF and H1F-α expression induced by IL-1ß in HaCaT cells.
Saponin extracts (ß-sitosterol, asiatic acid, asiaticoside and madecassoside)[24]	*Centella asiatica*	Male Sprague–Dawley rats weighing 250– 300 g- incision and burn wounds	10% topical solution once daily	Inflammatory & proliferative	Mild degree of swelling, accelerated re-epithelization and keratinization and marked hair growth in extract-treated wounds in rats.
Asiaticoside [25,26]	*Centella asiatica*	Guinea pigs (male,	0.4% topical	Proliferative	Accelerate re-epithelization and fibroblast

		300– 325 g)- cutaneous (full thickness, completely transdermal) circular wounds of 8 mm diameter Sprague Dawley male rats (150–180 g)- diabetes induced via streptozotocin injection Male Sprague Dawley rats (200–220 g)- circular, skin-deep wounds of 8 mm diameter	solution 0.2% topical solution twice daily	Inflammatory	proliferation in diabetic rats. Increase in hydroxyproline content and tensile strength of healed tissue. Increase in antioxidants in regenerated tissue of cutaneous wounds in rats at initial stage of healing: superoxide dismutase, catalase, glutathione (GSH) peroxidase, vitamin E and ascorbic acid. Significant decrease in lipid peroxide levels.
Madecassoside [27]	*Centella asiatica* Herbs	Male ICR mice (18 – 22 g), and male Sprague-Dawley rats, (180 – 220g)- burn wounds	24 mg/kg oral solution for 20 days	Inflammatory & proliferative	Limits infiltration of inflammatory cells enhances proliferation of fibroblasts and neo-vascularisation in treated skin of burn wounds in mice. Decrease in nitric oxide (NO) and malondialdehyde MDA (end product of lipid peroxidation) levels and increase in GSH and hydroxyproline levels in treated mice,
Astragaloside VI & Cycloastragenol-6-O-beta-D-glucoside [28]	Astragali Radix (Dried roots of A*stragalus membranaceus var.mongholicus*)	Male C57BL/6JNarl mice, (eight-week-old) (20–25g)- Staphylococcus aureus infected, non-infected traumatic wound models	10 mM in Vaseline. Dressing changed every 2 days	Proliferative and Remodeling	Promote angiogenesis and accelerate wound closure of both non-infected and staphylococcus-aureus infected wounds in mice. Improve migration and proliferation of HaCaT and HDF skin cells via activation of the EGFR/ERK signaling pathway.

Cycloastragenol [29]	Astragali Radix (Dried roots of A*stragalus membranaceus var.mongholicus*)	-	0.3mM	Proliferative	Promote migration and proliferation of human epidermal stem cells (EpSCs) by activating Wnt/ß-catenin pathway contributing to increased TERT expression in EpSCs.
Astragaloside IV [30]	*Astragalus membranaceus* (Fisch) Bge	-	40-160 µg/ml	Proliferative and remodeling	Attenuate LiCl induced S phase cell cycle arrest in keratinocytes. Promote migration and proliferation of keratinocytes by down-regulating ß-catenin expression and up-regulating proliferating cell nuclear antigen (PCNA) expression.
Lupeol [31,32]	*Bowdichia virgilioides*	Male Wistar rats (250 g ± 2 g)- full thickness excisional wound	*In vitro* 0.1-20 µg/ml *In vivo* 0.2% w/w lupeol cream	Inflammatory Proliferative	Reduce inflammation-upregulation of MMP-2 and reduced NF-κB expression *in vitro.* Reduced inflammatory cells infiltration, proinflammatory cytokine, IL6 and NF-κB expression, increased anti-inflammatory cytokine, IL-10 and SOD, HO-1 enzyme expression *in vivo.* Improved migration of human epidermal keratinocytes and expression of Akt, p38 and Tie-2 signaling proteins involved in cell proliferation, migration and angiogenesis *in vitro.* Increase migration and proliferation of fibroblasts and neovascularisation *in vivo* - strong expression of FGF-2, collagen type III and angiogenic growth factors, TGF-β1and Hif-1α.

Table S4. *In vivo* results of tannins and essential oils in wound healing

Molecule	Source	Wound healing models	Dosage	Wound healing phase	Action
Tannins					
Tannin extracts (81%) [33]	Immature fruits of Terminalia chebula Fructus Retz	Adult male Sprague-Dawley rats. (200-220g) Acute excision	5 mg	Inflammatory	Higher VEGFA mRNA expression and amount of newly formed capillaries during early stages of wound healing compared to erythromycin ointment and Vaseline. Antibacterial activity against staphylococcus aureus and Klebsiella pneumonia.
Tannic acid [34]	Solarbio Corp.	Male Sprague Dawley rats (200-220g)	*In vitro* 0.1-0.4 µg/ml *In vivo* 0.5-1.5 g/ml	Proliferative	Accelerated re-epithelization similar to Yunnan Baiyao treated group. Promote thin epidermis with well-formed hair follicles and organized collagen and reduce scarring. Higher expression of bFGF, TGF-ß, FN and VEGF.
Proanthocyanidin extract [35]	Grape seed	Male BalbC mice Full thickness excisional dermal wound model	25 µL of 100 mg/mL	Proliferative	Accelerated wound contraction and better organized regenerating tissue compared to placebo-treated wound. Upregulates VEGF transcription.
Essential Oils					
Carvacrol [36]	Sigma-Aldrich	Male wistar-albino rats Full-thickness skin wounds	200 µl of 12.5% in sunflower oil for 5 days	Proliferative	Increased granulation tissue by modulating TNF-α, IL-1ß and TGF-ß expressions
D-limonene [37]	Sigma-Aldrich	Hairless Skh1 female mice Inflammation induced daily using 12-O-Tetradecanoylphorbol-13-acetate dissolved in acetone Full thickness dorsal wound	10 mg/kg D-limonene in sunflower oil	Inflammatory	Accelerated wound closure. Anti-angiogenic effect. Reduce pro-inflammatory cytokines.

Limonene and fenchone (components of *Foeniculum vulgare)* [38]	Sigma-Aldrich	Male Sprague-Dawley rats Full thickness excisional wound model	1:1 mixture of limonene and/or fenchone in olive oil	Inflammatory & Proliferative	Promote regular and denser collagen deposition, enhance angiogenesis and improve re-epithelization
Sesquiterpenoids (cedrol and widdrol) [39]	*Juniperus occidentalis*	Male Sprague-Dawley rats Linear and circular dorsal wound models	1% w/w of test ointment (glycerol stearate, 1,2-propylene glycol and liquid paraffin)	Inflammatory & Proliferative	High hydroxyproline content and faster re-epithelization in *J.occidentalis* essential oil treated wounds.
Cinnamaldehyde (CA) [40]	Beijing Naturally Occurring Drugs Research Institute	Male diabetic (BSK.Cg-m+/+Lepr^{db};db/db) and WT mice. Full thickness dorsal wound model	25-100 mg/kg CA intraperitoneal injection.	Proliferative	Accelerated wound healing & promotion of angiogenesis via activation of PI3K and MAPK signaling pathways.
Trans-cinnamaldehyde [41]	Sigma-Aldrich	Female Swiss mice Full thickness dorsal skin wound inoculated with *P.aerudinosa*	30 µL of 0.5 mg/mL sterile cinnamaldehyde applied topically	Proliferative	Faster healing in treated mice. Reduction in secretion of VEGF, IL6, IL-17, and NO.
Cinnamon essential oil (54% cinnamic aldehyde, 12.3% α-copaene, 7% styrene, ethenyle, benzebe [42]	*Cinnamomum verum* bark	BALB/c mice Full thickness dorsal wound inoculated with *S.aureus* and *P. aeruginosa*	2-4% w/w oil in soft yellow paraffin	Proliferative	Upregulated VEGF, IGF-1 and FGF-2 expression in infected model. Increased collagen synthesis and re-epithelization.

References

1 J. Kurek, in *Alkaloids - Their Importance in Nature and Human Life*, IntechOpen, 2019.
2 A. N. Panche, A. D. Diwan and S. R. Chandra, *J. Nutr. Sci.*, 2016, 5, 1–15.
3 D. Kregiel, J. Berlowska, I. Witonska, H. Antolak, C. Proestos, M. Babic, L. Babic and B. Zhang, in *Application and Characterization of Surfactants*, IntechOpen, 2017.
4 A. Pizzi, in *Monomers, Polymers and Composites from Renewable Resources*, Elsevier Ltd, 2008, pp. 179–199.
5 J. Reichling, P. Schnitzler, U. Suschke and R. Saller, *Complement. Med. Res.*, 2009, **16**, 79–90.
6 J. P. Fetse, J. O. Kyekyeku, E. Dueve and K. B. Mensah, *Br. J. Pharm. Res.*, 2014, 2642–2652.
7 A. J. Vaisberg, M. Milla, M. C. Planas, J. L. Cordova, E. R. de Agusti, R. Ferreyra, M. C. Mustiga, L. Carlin and G. B. Hammond, *Planta Med.*, 1989, **55**, 140–143.
8 B. H. Porras-Reyes, T. A. Mustoe, W. H. Lewis, J. Roman and L. Simchowitz, *Proc. Soc. Exp. Biol. Med.*, 1993, **203**, 18–25.
9 S. Mahibalan, M. Stephen, R. T. Nethran, R. Khan and S. Begum, *Pharm. Biol.*, 2016, **54**, 2851–2856.
10 T. Nagappan, T. C. Segaran, M. E. A. Wahid, P. Ramasamy and C. S. Vairappan, *Molecules*, 2012, **17**, 14449–14463.
11 G. Yin, Z. Wang, Z. Wang and X. Wang, *Exp. Dermatol.*, 2018, **27**, 779–786.
12 J. Fu, J. Huang, M. Lin, T. Xie and T. You, *J. Surg. Res.*, 2019, **246**, 213–223.
13 V. Kant, B. L. Jangir, A. Nigam, V. Kumar and S. Sharma, *Wound Med.*, 2017, **19**, 82–87.
14 K. M. Doersch and M. K. Newell-Rogers, *Exp. Biol. Med.*, 2017, **242**, 1424–1431.
15 S. Lodhi and A. K. Singhai, *Asian Pac. J. Trop. Med.*, 2013, **6**, 253–259.
16 I. Süntar, E. Küpeli, H. Keles, E. Yesilada and S. D. Sarker, *J. Ethnopharmacol.*, 2013, **149**, 103–110.
17 Y. Ozay, S. Guzel, O. Yumrutas,, B. Pehlivanoglu, I. H. Erdogdu, Z. Yildirim, B. A. Turk and S. Darcan, *J. Surg. Res.*, 2019, **233**, 284–296.
18 S. Shan, Y. Zhang, M. I. N. Wu, B. O. Yi, J. Wang and Q. Li, *ACS Omega*, 2017, 4643–4649.
19 C. Cao, S. Li, X. Dai, Y. Chen, Z. Feng, Y. Zhao and J. Wu, 2009, **35**, 89–97.
20 L. Wang, T. He, A. Fu, Z. Mao and L. Yi, *Eur. J. Inflamm.*, , DOI:10.1177/2058739218775255.
21 S. Li, Y. Dang, X. Zhou, B. Huang, X. Huang, Z. Zhang, Y. W. Kwan, S. W. Chan, G. Pak, H. Leung, S. Ming, Y. Lee, M. Pui and M. Hoi, *Nat. Sci. Reports*, 2015, **5**, 16815.
22 Y. S. Kim, I. Cho, M. Jeong, S. Jeong, S. Y. Nah, Y. Cho, S. H. Kim, A. Go, S. E. Kim, S. S. Kang, C. J. Moon, J. C. Kim, S. H. Kim and C. S. Bae, 2011, **35**, 360–367.
23 Y. Kimura, M. Sumiyoshi, K. Kawahira and M. Sakanaka, *Br. J. Pharmacol.*, 2006, **148**, 860–870.
24 J. Somboonwong, M. Kankaisre, B. Tantisira and M. H. Tantisira, *BMC Complement. Altern. Med.*, , DOI:10.1186/1472-6882-12-103.
25 A. Shukla, A. M. Rasik, G. K. Jain, R. Shankar and D. K. Kulshrestha, *J. Ethnopharmacol.*, 1999, **65**, 1–11.
26 A. Shukla, A. M. Rasik and B. N. Dhawan, *Phyther. Res.*, 1999, **13**, 50–54.
27 M. Liu, Y. Dai, Y. Li, Y. Luo, F. Huang, Z. Gong and Q. Meng, *Planta Med.*, 2008, **74**, 809–815.
28 S. Lee, S. Lee, W. Chang, Z. Li, N. S. Kirkby and W. Tsai, *Phytomedicine*, 2019, **38**,

183–191.
29 Y. Cao, L. Xu, X. Yang, Y. Dong, H. Luo, F. Xing and Q. Ge, *Biomed Res. Int.*
30 F. L. Li, X. Li, Y. F. Wang, X. L. Xiao, R. Xu, J. Chen, B. Fan, W. Bin Xu, L. Geng and B. Li, *Evidence-based Complement. Altern. Med.*, , DOI:10.1155/2012/956107.
31 F. P. Beserra, M. Xue, G. Lemos, D. A. Maia, A. L. Rozza and C. J. Jackson, *Molecules*, 2018, **23**, 2819.
32 F. P. Beserra, A. J. Vieira, L. Fernando, S. Gushiken, E. O. De Souza, M. F. Hussni, C. A. Hussni, R. H. Nóbrega, E. Ricardo, M. Martinez, C. J. Jackson, G. Lemos, D. A. Maia, A. L. Rozza and C. H. Pellizzon, *Oxid. Med. Cell. Longev.*, , DOI:10.1155/2019/3182627.
33 K. Li, Y. Diao, H. Zhang, S. Wang, Z. Zhang, B. Yu, S. Huang and H. Yang, *BMC Complement. Altern. Med.*, 2011, **11**, 86.
34 Y. Chen, L. Tian, F. Yang, W. Tong, R. Jia, Y. Zou, L. Yin, L. Li, C. He, X. Liang, G. Ye, C. Lv, X. Song and Z. Yin, *Adv. Wound Care*, 2019, **8**, 341–354.
35 S. Khanna, M. Venojarvi, S. Roy, N. Sharma, P. Trikha, D. Bagchi, M. Bagchi and C. K. Sen, *Free Radic. Biol. Med.*, 2002, **33**, 1089–1096.
36 M. Y. Gunal, A. O. Heper and N. Zaloglu, *Pharmacogn. J.*, 2014, **6**, 10–14.
37 P. d'Alessio, M. Mirshahi, J.-F. Bisson and M. Bene, *Antiinflamm. Antiallergy. Agents Med. Chem.*, 2014, **13**, 29–35.
38 I. Keskin, Y. Gunal, S. Ayla, B. Kolbasi, A. Sakul, U. Kilic, O. Gok, K. Koroglu and H. Ozbek, *Biotech. Histochem.*, 2017, **92**, 274–282.
39 I. Tumen, I. Süntar, F. J. Eller, H. Keleş and E. K. Akkol, *J. Med. Food*, 2013, **16**, 48–55.
40 X. Yuan, L. Han, P. Fu, H. Zeng, C. Lv, W. Chang, R. S. Runyon, M. Ishii, L. Han, K. Liu, T. Fan, W. Zhang and R. Liu, *Lab. Investig.*, 2018, **98**, 783–793.
41 T. A. F. Ferro, E. B. Souza, M. A. M. Suarez, J. F. S. Rodrigues, D. M. S. Pereira, S. J. F. Mendes, L. F. Gonzaga, M. C. A. M. Machado, M. R. Q. Bomfim, J. B. Calixto, J. L. Arbiser, V. Monteiro-Neto, E. André and E. S. Fernandes, *Molecules*, 2019, **24**, 1627.
42 S. G. Seyed Ahmadi, M. R. Farahpour and H. Hamishehkar, *Kaohsiung J. Med. Sci.*, 2019, **35**, 686–694.