



Contents lists available at ScienceDirect

Integrative Medicine Research

journal homepage: www.imr-journal.com

Identification of candidate medicinal herbs for skincare via data mining of the classic *Donguibogam* text on Korean medicine

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ARTICLE INFO

Article history:

Received 6 April 2020

Received in revised form 26 May 2020

Accepted 26 May 2020

Available online 3 June 2020

Keywords:

Cosmetic development

Data mining

Skincare

Traditional herbal medicine

ABSTRACT

Background: Korean cosmetics are widely exported throughout Asia. Cosmetics exploiting traditional Korean medicine lead this trend; thus, the traditional medicinal literature has been invaluable in terms of cosmetic development. We sought candidate medicinal herbs for skincare.

Methods: We used data mining to investigate associations between medicinal herbs and skin-related keywords (SRKs) in a classical text. We selected 26 SRKs used in the *Donguibogam* text; these referred to 626 medicinal herbs. Using a term frequency-inverse document frequency approach, we extracted data on herbal characteristics by assessing the co-occurrence frequencies of 52 medicinal herbs and the 26 SRKs.

Results: We extracted the characteristics of the 52 herbs, each of which exhibited a distinct skin-related action profile. For example Ginseng Radix was associated at a high-level with tonification and anti-aging, but Rehmanniae Radix exhibited a stronger association with anti-aging. Of the 52 herbs, 46 had been subjected to at least one modern study on skincare-related efficacy.

Conclusions: We made a comprehensive list of candidate medicinal herbs for skincare via data mining a classical medical text. This enhances our understanding of such herbs and will help with discovering new candidate herbs.

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Introduction

It has been reported that 50% of British consumers prefer cosmetics made with natural ingredients.¹ This trend is not limited to the United Kingdom rather, it reflects customer demands for sustainable cosmetics free of harmful chemicals. Natural resources (“folk medicinal herbs”) have long been used as cosmetic ingredients worldwide. Mexicans applied *Matricaria chamomilla* L. to wounds and skin eruptions, and chamomile was also a popular medicinal plant in England, France, and Belgium.² In Italy, oint-

ment made from the flowers of the pot marigold was used to treat reddened skin, and lavender macerated in cold water was used to tonify skin.³ Indians mix various herbs including neem (*Azadirachta indica* A.Juss.) into pastes for skin rejuvenation.⁴ In South Africa, the leaves of aloe vera (*Aloe arborescens* Mill.) have been topically applied to wounds and burns, and the roots and leaves of river pumpkin (*Gunnera perpersa* L.) have been employed to dress psoriasis.⁵ Many of these plants remain widely used as cosmetic ingredients.

Korean traditional medical books deal extensively with skin remedies and cosmetics; this has aided the Korean herbal cosmetics industry. Goji berries make the face appear youthful, and face-washing with peach blossoms is thought to be beautifying.⁶ The Korean medical classic, the *Donguibogam*, also contains a large amount of relevant information. Previous reviews extracted various skin-related prescriptions that were evaluated both *in vitro* and *in vivo* in terms of herbal and formulaic efficacies when used as cosmetics or ointments.⁷ Recently, computer-aided approaches have been used to study Korean traditional medicine.⁸ The analysis of *Donguibogam* terms led to the discovery of novel

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Table 1
Skin-Related Keywords (SRKs).

No.	SRK	Details	Skincare Function Category
1	Dryness	17 terms describing skin dryness, roughness, cracking, and flaking	Hydration
2	Itchiness	13 terms describing itchiness	
3	Gloss	12 terms describing skin gloss, shine, luster, and sheen	
4	Enrichment	5 terms describing skin fullness, fatness, lubriciousness, and substance	Whitening
5	Pigmentation	28 terms describing hyperpigmentation, freckles, and age spots	
6	Complexion	35 terms describing skin color and blemishes	
7	Dyspigmentation	6 terms describing dyspigmentation, vitiligo, and melioma	Tonification
8	Rosacea	10 terms describing rosacea	
9	Tonification	22 terms describing an energetic appearance, vitality, a thin-faced impression, and a haggard appearance	
10	Rejuvenation	17 terms describing anti-aging, rejuvenation, and longevity	Anti-aging
11	Wrinkle	3 terms describing skin folds and wrinkles	
12	Scar	3 terms describing scars	
13	Wound adhesion	11 terms describing wound-healing and regeneration	
14	Injury treatment	16 terms describing treatments for various injuries	
15	Exfoliate	12 terms describing skin hyperplasia	
16	Deinsectization	12 terms describing bug bites	
17	Detoxification	toxins or bodily wastes in combination with other SRKs	Anti-inflammatory
18	Purification	7 terms describing body and clothing decontamination	
19	Abscess and carbuncle	6 terms describing abscesses and carbuncles	
20	Miscellaneous	34 terms describing acne, hives, and dermatitis, but not abscesses and carbuncles	
21	Pus	6 terms describing pus formation	
22	Soothing	3 terms describing heat in combination with other SRKs	
23	Pain on skin	pain in combination with other SRKs	
24	Edema	4 terms describing edema	
25	Circulation related to skin	13 terms describing circulation in combination with other SRKs	
26	Numbness	4 terms describing numbness in combination with other SRKs	

candidate cognition-enhancing herbs,^{9,10} candidate anti-aging herbs,¹¹ stroke treatments,¹² and prescriptions for Parkinson-type rigidity.¹³ However, to the best of our knowledge, no study has yet used data mining to comprehensively analyze Donguibogam cosmetic prescriptions.

We found medicinal herbs that were effective for skincare, focusing on previously neglected herbs with novel skin benefits. From there, we assembled a comprehensive list of medicinal herbs with cosmetic potential. Our work both adds to the body of knowledge regarding traditional literature and aids cosmetic companies.

Methods

Skincare-related terms

All prescriptions featuring words associated with the skin were analyzed. Experts in Korean medicine, cosmetics, data science, and medical history decided (G.C., W.M.J, and W.C) on 26 representative skin-related keywords (SRKs) after discussion. The keywords referred to a bodily region (face, skin, scalp, and hair), efficacy (cleaning, moisturizing, whitening, and anti-aging), and usage (cleansers, facial oils, and ointments). We linked the SRKs to five major cosmetic functions (hydration, whitening, tonification, anti-aging, and anti-inflammation) (Table 1). Tonification can be translated as “energy-boosting,” embracing the concepts of defense system-boosting and anti-fatigue activity. We considered tonification to be a functional skincare category.

Data collection and pre-processing

We extracted 3,912 compounded prescriptions in which 1,041 herbs appeared 28,183 times. The herb number fell to 1,029 after herbal name pre-processing. Of the 1,029 herbs, we identified 626 present in prescriptions that included at least one of the 26 SRKs. Of these, 322 appeared more than 10 times; we confined our attention to these (Fig. 1).

Data mining

We applied a term frequency-inverse document frequency (tf-idf) weighting scheme to the co-occurrence table.¹⁴ We first created a co-frequency table of SRKs and compounded prescriptions. We also prepared a co-frequency table of compounded prescriptions and herbs. The co-frequency table of SRKs and herbs was the dot product of the two co-frequency tables mentioned above. The co-frequencies between herbs and compounded prescriptions were divided by $\log(1 + \text{the number of herbs in each prescription})$. Based on the co-frequency table, a tf-idf value for each herb was calculated by assigning the Document descriptor to herbs and the Term descriptor to the SRK categories. The tf-idf value of the category for each herb was L2-normalized

Statistical analysis

The permutation test was used to reveal significant associations between medicinal herbs and the SRKs. The SRK list of the compounded prescriptions was randomly permuted. The resulting tf-idf values between the herbs and the SRKs were calculated, and the process was repeated 10,000 times to obtain a null distribution of the tf-idf values. P-values were calculated based on the locations of true observations within the simulated null distribution. As the SRK tf-idf values were tested separately for each herb, we corrected for multiple testing using the Benjamini-Hochberg false-discovery rate. The statistical relevance of each SRK was presented as a Z-score calculated using the null distribution from the permutation test.

Results

A total of 52 medicinal herbs were extracted from the Donguibogam

A total of 52 medicinal herbs were significantly linked to the 26 SRKs (tf-idf index p -values <0.05); a color-coded summary is shown in Fig. 2. The SRKs lie on the x-axis and the relevant herbs

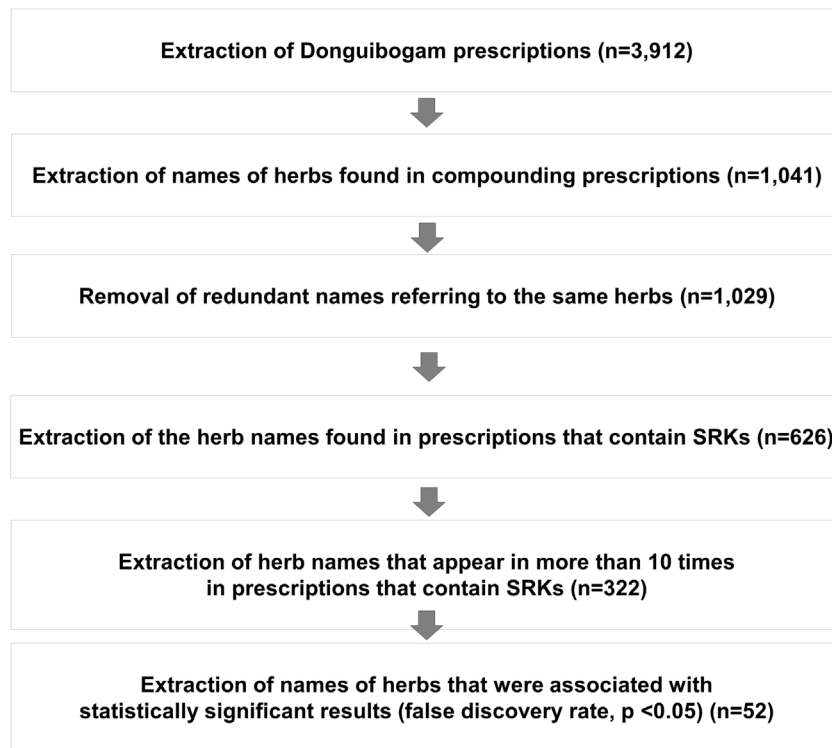


Fig. 1. Process of extraction of names of medicinal herbs associated with skin related-keywords (SRKs).

Table 2

The 52 candidate medicinal herbs found via data mining.

Skincare Function	Skin-Related Keyword	Medicinal herbs identified
Hydration	Itchiness	Osterici Radix, Gastrodiae Rhizoma, Cinnamomi Ramulus, Polyporus, Plantaginis Semen
	Gloss	Schisandrae Fructus
Whitening	Complexion	Massa Medicata Fermentata, Hordei Fructus Germinatus, Amomi Tsao-ko Fructus, Asini Corii Colla, Dolichoris Semen
	Dyspigmentation	Acori Graminei Rhizoma, Chrysanthemi Flos
Tonification	Rosacea	Inulae Flos
	Tonification	Ginseng Radix, Atractylodis Rhizoma Alba, Dioscoreae Rhizoma, Eucommiae Cortex, Cistanches Herba, Morindae Radix, Cervi Parvum Cornu, Zingiberis Rhizoma, Aconiti Lateralis Radix Preparata, Alpiniae Officinari Rhizoma, Hoelen, Schisandrae Fructus, Massa Medicata Fermentata, Polygalae Radix, Achyranthis Radix
Anti-Aging	Rejuvenation	Ginseng Radix, Rehmanniae Radix, Liriopsis Tuber, Asparagi Tuber, Lycii Fructus, Cuscutae Semen, Nelumbinis Semen, Lycii Radicis Cortex, Euphorbiae Kansui Radix
	Wrinkles	Mume Fructus
	Exfoliation	Cyperis Rhizoma
	Deinsectization	Piperis Longi Fructus
	Abscess	Astragali Radix, Magnoliae Cortex, Cinnamomi Cortex, Succinum, Alpiniae Katsumadai Semen, Crotonis Semen
Anti-inflammation	Miscellaneous	Perillae Folium
	Soothing quality	Scutellariae Radix, Gypsum Fibrosum
	Pain	Persicae Semen, Curcumae longae Rhizoma
	Edema	Raphani Semen
	Circulation	Arisaematis Rhizoma, Jujubae Fructus
	Numbness	Atractylodis Rhizoma Alba, Aconiti Lateralis Radix Preparata, Amomi Tsao-ko Fructus

are indicated on the y-axis. Herbs exhibiting significant associations with the 26 SRKs are shown in different colors. For example, *Panax ginseng* C.A.Mey. (Ginseng Radix) was markedly associated with tonification and anti-aging, but *Rehmannia glutinosa* (Gaertn.) DC. (Rehmanniae Radix) was significantly associated with anti-aging only. The medicinal herbs and their associated SRKs are listed in Table 2.

Medicinal herbs related to hydration

Six medicinal herbs were associated with hydration: root of *Notopterygium incisum* K.C.Ting ex H.T.Chang (Osterici Radix) ($Z = 5.87$), stem bark of *Cinnamomum cassia* (L.) J.Presl (Cinnamomi

Ramulus) ($Z = 4.67$), seed of *Plantago asiatica* L. (Plantaginis Semen) ($Z = 3.99$), sclerotium of *Polyporus umbellatus* Fries (Polyporus) ($Z = 4.32$), rhizome of *Gastrodia elata* Blume (Gastrodiae Rhizoma) ($Z = 4.89$), and fruit of *Schisandra chinensis* (Turcz.) Baill. (Schisandrae Fructus) ($Z = 7.36$). Of the six, Osterici Radix, Cinnamomi Ramulus, Plantaginis Semen, Polyporus, and Gastrodiae Rhizoma were linked to "itchiness" and Schisandrae Fructus to "gloss."

Medicinal herbs related to whitening

Eight medicinal herbs were associated with whitening: Massa Medicata Fermentata ($Z = 4.70$), germinated seed of *Hordeum*

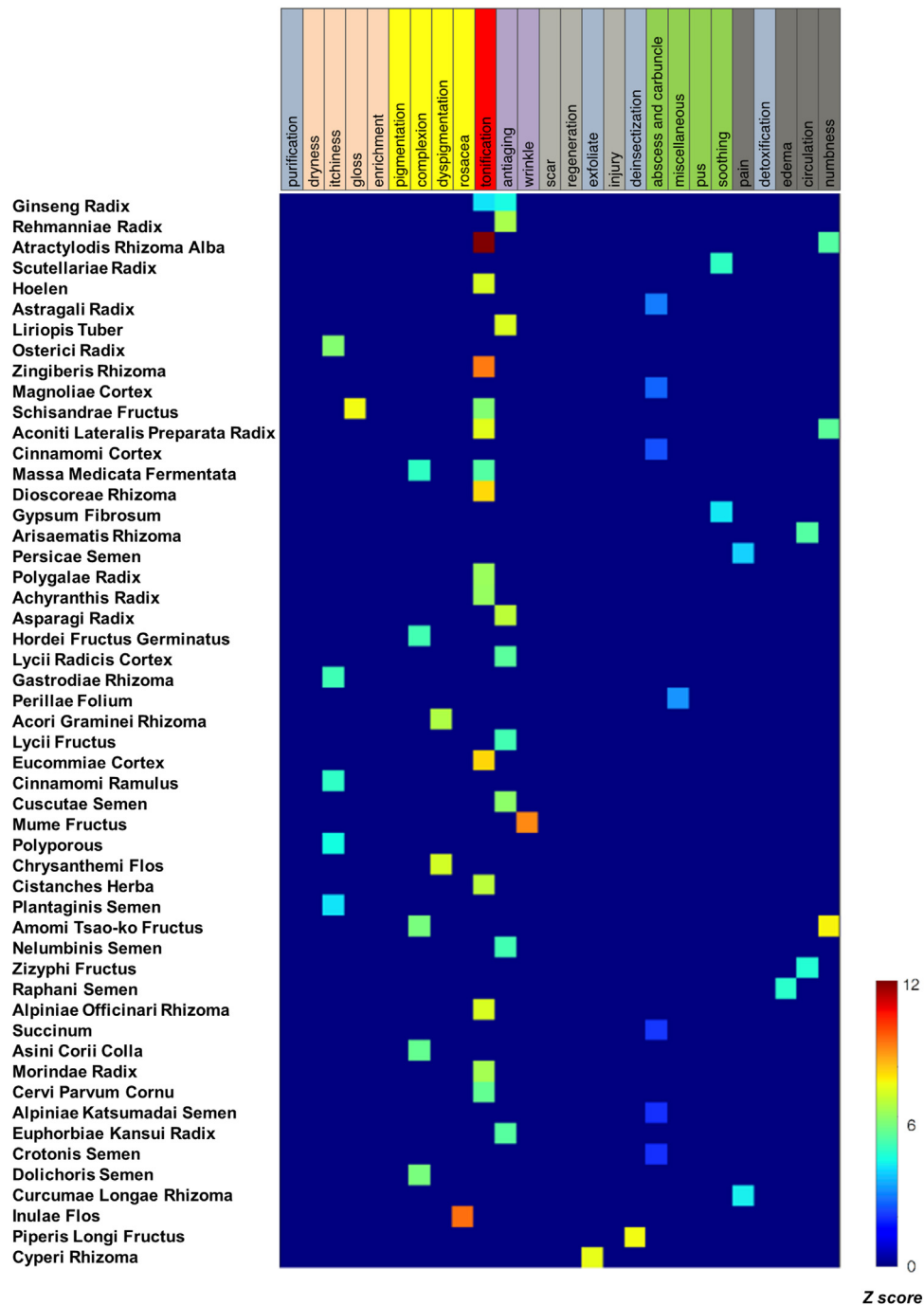


Fig. 2. A color-coded map of the relationships between the 52 herbs and 26 SRKs. We used data mining to reveal the characteristics of 52 herbs mentioned in a classical medical text. Each herb is associated with a different skin-related function. For example, Ginseng Radix was highly associated with both tonification and anti-aging, but Rehmanniae Radix was associated with anti-aging only.

vulgare L. (Hordei Fructus Germinatus) ($Z = 4.94$), stewing and concentrating material from *Equus asinus* L. (Asini Corii Colla) ($Z = 5.42$), seed of *Dolichos lablab* L. (Dolichoris Semen) ($Z = 5.69$), rhizome of *Acorus gramineus* Aiton (Acori Gramineri Rhizoma) ($Z = 6.44$), flower of *Chrysanthemum indicum* L. (Chrysanthemi Flos) ($Z = 6.89$), fruit of *Amomum tsao-ko* Crevost & Lemarié (Amomi Tsao-ko Fructus) ($Z = 5.70$), and flower of *Inula britannica* L. (Inulae Flos) ($Z = 9.03$). Inulae Flos was the only herb associated with “rosacea.” Both Acori Gramineri Rhizoma and Chrysanthemi Flos were associated with “dyspigmentation.” The other five herbs were associated with “complexion.”

Medicinal herbs related to tonification

Fifteen medicinal herbs were associated with tonification: Ginseng Radix ($Z = 3.98$), rhizome of *Atractylodes macrocephala* Koidz. (Atractylodis Rhizoma Alba) ($Z = 11.44$), sclerotium of *Poria cocos* Wolf (Hoelen) ($Z = 6.96$), rhizome of *Zingiber officinale* Roscoe (Zingiberis Rhizoma) ($Z = 8.90$), Schisandrae Fructus ($Z = 5.84$), processed lateral root of *Aconitum carmichaeli* Debeaux (Aconiti Lateralis Radix Preparata) ($Z = 7.13$), Massa Medicata Fermentata ($Z = 5.17$), rhizome of *Dioscorea japonica* Thunb. (Dioscoreae Rhizoma) ($Z = 7.76$), root of *Polygala tenuifolia* Willd. (Polygalae Radix) ($Z = 6.16$), root of *Achyranthes bidentata* Blume (Achyranthis Radix)

(Z = 6.12), cortex of *Eucommia ulmoides* Oliv. (Eucommiae Cortex) (Z = 7.78), stem of *Cistanche deserticola* Y.C.Ma (Cistanches Herba) (Z = 6.58), rhizome of *Alpinia officinarum* Hance (Alpiniae Officinari Rhizoma) (Z = 6.99), root of *Morinda officinalis* F.C.How (Morindae Radix) (Z = 6.29), and pilose antler of *Cervus nippon* Temminck (Cervi Parvum Cornu) (Z = 5.39).

Medicinal herbs related to anti-aging

Ten medicinal herbs were associated with anti-aging: Ginseng Radix (Z = 4.26), Rehmanniae Radix (Z = 6.36), tuberous root of *Ophiopogon japonicus* (Thunb.) Ker Gawl. (Liriopsis Tuber) (Z = 7.05), tuberous root of *Asparagus cochinchinensis* (Lour.) Merr. (Asparagi Tuber) (Z = 6.64), root cortex of *Lycium barbarum* L. (Lycii Radicis Cortex) (Z = 5.25), fruit of *Lycium barbarum* L. or *Lycium chinense* Mill. (Lycii Fructus) (Z = 4.94), seed of *Cuscuta chinensis* Lam. (Cuscutae Semen) (Z = 5.98), seed of *Nelumbo nucifera* Gaertn. (Nelumbinis Semen) (Z = 4.92), fruit of *Prunus mume* (Siebold) Siebold & Zucc. (Mume Fructus) (Z = 8.74), and root of *Euphorbia kansui* S.L.Liou ex S.B.Ho (Euphorbiae Kansui Radix) (Z = 5.22). Mume Fructus was the only herb in the “wrinkle” subgroup; the other herbs belonged to the “rejuvenation” subgroup.

Medicinal herbs related to anti-inflammation

A total of 19 medicinal herbs were associated with anti-inflammation: rhizome of *Cyperus rotundus* L. (Cyperii Rhizoma) (Z = 7.22), fruit of *Piper longum* L. (Piperis Longi Fructus) (Z = 7.35), root of *Astragalus membranaceus* (Fisch.) Bunge (Astragali Radix) (Z = 2.86), cortex of *Magnolia officinalis* Rehder & E.H.Wilson (Magnoliae Cortex) (Z = 2.58), cortex of *Cinnamomum cassia* (L.) J.Presl (Cinnamomi Cortex) (Z = 2.34), Succinum (Z = 2.08), seed of *Alpinia katsumadai* Hayata (Alpiniae Katsumadai Semen) (Z = 1.99), seed of *Croton tiglium* L. (Crotonis Semen) (Z = 2.01), leaf of *Perilla frutescens* (L.) Britton (Perillae Folium) (Z = 3.10), root of *Scutellaria baicalensis* Georgi (Scutellariae Radix) (Z = 4.73), Gypsum Fibrosum (Z = 4.05),

seed of *Prunus persica* (L.) Batsch (Persicae Semen) (Z = 3.76), rhizome of *Curcuma longa* L. (Curcumae Longae Rhizoma) (Z = 4.14), seed of *Raphanus sativus* L. (Raphani Semen) (Z = 4.58), rhizome of *Arisaema amurense* Maxim. (Arisaematis Rhizoma) (Z = 5.16), fruit of *Ziziphus jujuba* Mill. (Jujubae Fructus) (Z = 4.50), *Atractylodis Rhizoma Alba* (Z = 5.14), *Aconiti Lateralis Radix Preparata* (Z = 5.30), and *Amomi Tsao-ko Fructus* (Z = 7.43).

Cyperii Rhizoma was associated with the term “exfoliate”; *Piperis Longi Fructus* with “deinsectization”; *Astragali Radix*, *Magnoliae Cortex*, *Cinnamomi Cortex*, *Succinum*, *Alpiniae Katsumadai Semen*, and *Crotonis Semen* with “abcess”; *Perillae Folium* with “miscellaneous”; *Scutellariae Radix* and *Gypsum Fibrosum* with “soothing”; *Persicae Semen* and *Curcumae Longae Rhizoma* with “pain”; *Raphani Semen* with “edema”; *Arisaematis Rhizoma* and *Jujubae Fructus* with “circulation”; and *Atractylodis Rhizoma Alba*, *Aconiti Lateralis Radix Preparata*, and *Amomi Tsao-ko Fructus* with “numbness.”

Medicinal herbs related to more than one skincare function

Of the 52 medicinal herbs, six were associated with two skincare functions: *Schisandrae Fructus* with hydration and tonification, *Massa Medicata Fermentata* with whitening and tonification, *Amomi Tsao-ko Fructus* with whitening and anti-inflammation, *Atractylodis Rhizoma Alba* and *Aconiti Lateralis Radix Preparata* with anti-inflammation and tonification, and *Ginseng Radix* with anti-aging and tonification.

Literature review of the efficacies of the 52 candidate herbs

To verify the efficacies of the 52 candidate herbs, we performed a brief literature review. We found at least one example each of reported skincare efficacy for 46 herbs (Table 3). The six exceptions were *Aconiti Lateralis Preparata Radix*, *Arisaematis Rhizoma*,

Table 3

The skincare-related functions associated with the 52 candidate medicinal herbs.

No.	Candidate herb	Expected skin-related function	Reported skincare-related efficacy
1	<i>Achyranthis Radix</i>	Tonification	<i>Achyranthes bidentata</i> polysaccharide (ABP) and <i>Lycium barbarum</i> polysaccharide (LBP) inhibited nonenzymic glycation in a D-galactose-induced model of mouse aging; ABP was more effective than LBP. ²³
2	<i>Aconiti Lateralis Radix Preparata</i>	Tonification, Anti-inflammation	None. * Not an appropriate cosmetic ingredient (safety concerns).
3	<i>Acori Graminei Rhizoma</i>	Whitening	An <i>Acorus gramineus</i> extract inhibited tyrosinase activity and melanin synthesis. ²⁴
4	<i>Alpiniae Katsumadai Semen</i>	Anti-inflammation	An <i>Alpinia katsumadai</i> Hayata methanol extract reduced house dust mite-induced atopic dermatitis in NC/Nga mice. ²⁵
5	<i>Alpiniae Officinari Rhizoma</i>	Tonification	An 80% (v/v) aqueous acetone extract from rhizomes of <i>Alpinia officinarum</i> inhibited melanogenesis in mice with theophylline-stimulated murine B16 melanomas. ²⁶
6	<i>Amomi Tsao-ko Fructus</i>	Whitening Anti-inflammation	Catechins and catechol derivatives from the fruit of <i>Amomum tsao-ko</i> exhibited strong DPPH radical-scavenging and antioxidant activities. 2,8-decadiene-110-diol from <i>Amomum tsao-ko</i> extract inhibited the production of nitric oxide (NO) and prostaglandin E2 by downregulating NO synthase and COX-2 expression. ¹⁰
7	<i>Arisaematis Rhizoma</i>	Anti-inflammation	None. * Not an appropriate cosmetic ingredient (safety concerns).
8	<i>Asini Corii Colla</i>	Whitening	None.
9	<i>Asparagi Tuber</i>	Anti-Aging	An aqueous extract of <i>Asparagus cochinchinensis</i> (Lour.) Merr. shoots exhibited strong radical-scavenging capacities <i>in vivo</i> and <i>in vitro</i> . ²⁷
10	<i>Astragali Radix</i>	Anti-inflammation	<i>Astragalus sinicus</i> L. may ameliorate chronic inflammatory skin diseases by virtue of its antioxidant and anti-inflammatory activities; the material regulated intracellular reactive oxygen species (ROS) production; the NF-κB, JAK/STAT, and PI3/Akt signaling cascades; and immune responses. ²⁸
11	<i>Atractylodis Rhizoma Alba</i>	Tonification, Anti-inflammation	A compound from rhizomes of <i>A. macrocephala</i> inhibited NO production in a dose-dependent manner. ²⁹
12	<i>Cervi Parvum Cornu</i>	Tonification	A pharmacopuncture solution of <i>Cervi Pantotrichum Cornu</i> inhibited elastase activity and exhibited DPPH free radical-scavenging capacity. ³⁰
13	<i>Chrysanthemi Flos</i>	Whitening	Methanol and water extracts of <i>Chrysanthemum indicum</i> dose-dependently inhibited mushroom tyrosinase activity; the effects of the methanol extract were similar to those of kojic acid, a well-known tyrosinase inhibitor. ³¹
14	<i>Cinnamomi Cortex</i>	Anti-inflammation	<i>Cinnamomum cassia</i> bark that had undergone solid-state fermentation by <i>Phellinus baumii</i> reduced IL-31 expression in DNFB-treated C57BL/6 mice. ³²
15	<i>Cinnamomi Ramulus</i>	Hydration	<i>Cinnamomum cassia</i> extract inhibited the development of atopic dermatitis-like skin lesions in NC/Nga mice by suppressing the T-helper 2 cell response. ³³

Table 3 (Continued)

No.	Candidate herb	Expected skin-related function	Reported skincare-related efficacy
16	Cistanches Herba	Tonification	A phenylethanoid-rich extract from <i>Cistanche deserticola</i> exhibited antifatigue activity. ³⁴
17	Crotonis Semen	Anti-inflammation	Deep facial peeling using a mixture of low concentrations of phenol and croton oil improved wrinkles, eyelid tightening, and skin pigmentation. ³⁵ * Not an appropriate cosmetic ingredient (safety concerns).
18	Curcumae longae Rhizoma	Anti-inflammation	A hot-water extract of <i>Curcuma longa</i> significantly inhibited UVB-induced increases in tumor necrosis factor (TNF) α and interleukin (IL)-1 β at the mRNA and protein levels. ³⁶
19	Cuscutae Semen	Anti-Aging	An ethanol extract of <i>Cuscuta chinensis</i> exhibited antioxidant activity. ³⁷
20	Cyperi Rhizoma	Anti-inflammation	Valencene (VAL) from <i>Cyperus rotundus</i> inhibited TNF- α /IFN- γ -induced activation of NF- κ B. ³⁸
21	Dioscoreae Rhizoma	Tonification	An extract of aerial bulblets of <i>Dioscorea japonica</i> Thunb inhibited NF- κ B and MAPK signaling in RAW 264.7 cells. ³⁹
22	Dolichoris Semen	Whitening	None.
23	Eucommiae Cortex	Tonification	Pretreatment with aucubin from <i>Eucommia ulmoides</i> suppressed UVB-induced oxidative stress in the HaCaT cell line. ⁴⁰
24	Euphorbiae Kansui Radix	Anti-Aging	None * Not an appropriate cosmetic ingredient (safety concerns).
25	Gastrodiae Rhizoma	Hydration	4-hydroxybenzaldehyde accelerated acute wound-healing via activation of focal adhesion signaling in keratinocytes. ⁴¹
26	Ginseng Radix	Tonification	Panax ginseng berry/gold nanoparticles exhibited radical-scavenging, whitening, and moisture-retention activities. ⁴²
		Anti-Aging	<i>Panax ginseng</i> C.A. Meyer root extract (PGRE) activated the human COL1A2 promoter in a concentration-dependent manner. Human Type I procollagen synthesis was also induced by PGRE. ¹⁵
27	Gypsum Fibrosum	Anti-inflammation	Byakko-ka-ninjin-to (BN) (a prescription composed of the root of anemarrhena, ginseng, licorice, and rice) inhibited itchiness in an NC mouse model of atopic dermatitis. ⁴³
28	Hoelen	Tonification	Hoelen significantly inhibited melanin synthesis via the inhibition of TRP-2 expression. ⁴⁴
29	Hordei Fructus Germinatus	Whitening	A compound isolated from young green barley (<i>Hordeum vulgare</i> L.) inhibited melanin biosynthesis in B16 melanoma cells. ⁴⁵
30	Inulae Flos	Whitening	Sesquiterpenes from <i>Inula britannica</i> inhibited melanin synthesis by suppressing tyrosinase expression via ERK and Akt signaling. ⁴⁶
31	Jujubae Fructus	Anti-inflammation	An essential oil from <i>Zizyphus jujube</i> inhibited skin inflammation in an animal model. ⁴⁷
32	Liriopeis Tuber	Anti-Aging	Application of 0.5% (w/v) retinol, bakuchiol, an <i>Ophiopogon japonica</i> root extract cream, and 30% (w/v) vitamin C improved skin firmness and reduced wrinkles and hyperpigmentation. ⁴⁸
33	Lycii Fructus	Anti-Aging	Mice consuming goji berry (<i>Lycium barbarum</i>) juice were protected from UV radiation-induced skin damage via an antioxidant pathway. ¹⁶
34	Lycii Radicis Cortex	Anti-Aging	<i>Lycium barbarum</i> polysaccharide protected human keratinocytes against UVB-induced photo-damage. ⁴⁹
35	Magnoliae Cortex	Anti-inflammation	Magnoliae Cortex exerted an anti-inflammatory effect on <i>Porphyromonas gingivalis</i> -stimulated RAW 264.7 cells. ⁵⁰
36	Massa Medicata Fermentata	Tonification	<i>Triticum aestivum</i> L. exerted protective effects in an experimental animal model of chronic fatigue syndrome. ⁵¹
		Whitening	<i>Triticum aestivum</i> sprout extract attenuated 2,4-dinitrochlorobenzene-induced atopic dermatitis-like skin lesions in mice and chemokine expression in human keratinocytes. ⁵²
37	Morindae Radix	Tonification	Polysaccharides from the roots of <i>Morinda officinalis</i> exhibited anti-fatigue effects in mice. ⁵³ A methanol extract of the roots of <i>Morinda officinalis</i> exhibited anti-inflammatory and antinociceptive activities, inhibiting iNOS, COX-2, and TNF- α expression by downregulating NF- κ B binding activity. ⁵⁴
38	Mume Fructus	Anti-Aging	A <i>Prunus mume</i> extract exhibited a DPPH free radical-scavenging effect. ⁵⁵
39	Nelumbinis Semen	Anti-Aging	<i>Nelumbo nucifera</i> leaf protected against UVB-induced wrinkle formation and loss of subcutaneous fat by suppressing MCP3, IL-6, and IL-8 expression. ¹⁸
40	Osterici Radix	Hydration	An aqueous extract of <i>Rhizoma notopterygii</i> inhibited contact sensitivity by decreasing cytokine localization at the inflammation site; the extract also downregulated matrix metalloproteinase (MMP) activity. ⁵⁶
41	Perillae Folium	Anti-inflammation	Luteolin from perilla (<i>Perilla frutescens</i> L.) inhibited the secretion of inflammatory cytokines including IL-1 β and TNF- α from human mast cells. ⁵⁷
42	Persicae Semen	Anti-inflammation	Topical or oral administration of peach flower extract attenuated UV-induced epidermal thickening, MMP-13 expression, and pro-inflammatory cytokine production in the skin of hairless mice. ⁵⁸
43	Piperis Longi Fructus	Anti-inflammation	Piperlonguminine from <i>Piper longum</i> inhibited melanin production in melanoma B16 cells. ⁵⁹
44	Plantaginis Semen	Hydration	Plantamajoside from <i>Plantago asiatica</i> inhibited UVB- and advanced glycation end-products-induced MMP-1 expression by suppressing the MAPK and NF- κ B pathways in HaCaT cells. ⁶⁰
45	Polygalae Radix	Tonification	<i>Polygala tenuifolia</i> extract significantly inhibited HMC-1 cell degranulation and alleviated IMO stress-exacerbated atopic dermatitis symptoms by modulating the PKA/p38 MAPK signaling pathway. ⁶¹
46	Polyporus	Hydration	<i>Polyporus sclerotium</i> exhibited anti-UV activity; this ranked second among 25 herbs evaluated. ⁶²
47	Raphani Semen	Anti-inflammation	Compounds from <i>Raphanus sativus</i> seeds inhibited NO production in lipopolysaccharide-activated BV-2 cells. ⁶³
48	Rehmanniae Radix	Anti-Aging	Topical application of <i>Rehmannia glutinosa</i> extract inhibited mite allergen-induced atopic dermatitis in NC/Nga mice. ⁶⁴
49	Schisandrae Fructus	Hydration Tonification	Schisandrin from the fruit of <i>Schisandra chinensis</i> exhibited anti-inflammatory properties. ⁶⁵ Deoxyschisandrin and schisandrin B, the two major lignans of <i>Schisandra chinensis</i> , protected HaCaT cells from UVB-induced cell death by antagonizing the UVB-mediated production of ROS and induction of DNA damage. ⁶⁶
50	Scutellariae Radix	Anti-inflammation	A <i>Scutellaria baicalensis</i> 80% (v/v) ethanol extract exhibited anti-allergic effects on inflammation both <i>in vivo</i> and <i>in vitro</i> . ¹⁷
51	Succinum	Anti-inflammation	None.
52	Zingiberis Rhizoma	Tonification	A clinical trial enrolling 80 postmenopausal women showed that capsules containing 40 mg of <i>Tribulus terrestris</i> , 12.27 mg of <i>Zingiber officinale</i> , 3 mg of a <i>Crocus sativus</i> extract, and 11 mg of <i>Cinnamomum zeylanicum</i> improved menopausal symptoms. ⁶⁷

Asini Corii Colla, Dolichoris Semen, Euphorbiae Kansui Radix, and Succinum.

Discussion

We compiled a comprehensive list of candidate medicinal herbs for skincare by analyzing terms employed in the Donguibogam and identified the characteristics of 52 such herbs using SRKs. Each herb exhibited a different skincare function. Our findings will guide the development of new skincare products *via* experimental and clinical studies.

The Donguibogam is the most important classical text on medicinal practices in East Asia. A systematic search using data mining was productive.⁸ Ninety-seven candidate anti-aging herbs were identified through the data mining process, and 47 of those were selected for further analysis.¹¹ Ten herbs listed in the Donguibogam have been used to treat Parkinson-like rigidity.¹³ Combinations of 13 herbs have been used to treat stroke.¹² Additionally, 14 of 23 herbs that enhance cognition have been evaluated experimentally and clinically.^{9,10} In the current study, we found 52 skincare herbs and reviewed the modern literature for reports regarding these herbs. Recently, 46 herbs had been bio-medicinally evaluated in terms of skincare or related effects.

We prepared a list of herbs that had been subjected to efficacy testing. Some known efficacies were confirmed. For example, Ginseng Radix¹⁵ and Lycii Fructus were reported to exert anti-aging effects.^{15,16} Most reports studied skin cells *in vitro* or *in vivo*, and evidence of dermal efficacy was also evaluated. For example, Scutellariae Radix was associated with anti-inflammatory (a data-mining keyword) activity, and an 80% (v/v) ethanol extract of *Scutellaria baicalensis* exhibited anti-allergic effects both *in vivo* and *in vitro*.¹⁷ Nelumbinis Semen exerts an anti-aging effect, and *Nelumbo nucifera* leaf protects against UVB-induced wrinkle formation.¹⁸ Only six herbs have not been recently evaluated in terms of skin effects: Aconiti Lateralis Radix Preparata, Arisaematis Rhizoma, Asini Corii Colla, Dolichoris Semen, Euphorbiae Kansui Radix, and Succinum. Notably, four of these (Aconiti Lateralis Radix Preparata, Arisaematis Rhizoma, Crotonis Semen, and Euphorbiae Kansui Radix) are widely known to be toxic. Our approach affords a novel understanding of unknown medicinal characteristics of herbs used for skincare and will help in the identification of new skincare candidates.

Of the 52 candidate medicinal herbs, six were associated with two skincare functions. In Western medicine, one medicine is typically prescribed to treat a specific disease, whereas herbal mixtures are used in traditional East Asian medicine.¹² Natural products exert their therapeutic effects by acting on multiple targets.¹⁹ A multi-component multi-target approach lies at the core of medicinal herb pharmacology.²⁰ The different bodily perceptions of the East and West may render it difficult to integrate groups of skin-active herbs. In this sense, our first achievement was to define functional terms associated with skincare. We classified SRKs not by specific disease names, but rather on a holistic basis (in terms of affected bodily parts, functions, and applications). The candidate herbs and prescriptions were thus functionally defined, enhancing our understanding of the potential benefits of these herbs. Herbal functions and characteristics can then be quantitatively compared. We believe that our novel approach will aid the development of natural ingredients.

Natural products have been invaluable as a source of therapeutic agents.¹⁴ An herbal formula is not just addition of individual herbs, and it can produce greater effect than the sum of its individual constituents.²¹ Toxicity of toxic ingredients can be reduced and new active compounds can be more effective by combination formulas.²² Under the paradigm of network pharmacology, combi-

nations of multiple compounds can exert their therapeutic effects by acting on multiple targets.¹⁹ The most frequently used medicinal herb combinations can constitute a candidate group for the development of a new prescription for universal application.^{12,13} The ancient practice of combining multiple drugs in prescription formulas can provide us a practical guide for the development of the cosmetic ingredient for skincare. Further studies are necessary to identify multiple target components of the medicinal herbs by applying network pharmacological analysis.

Our work had several limitations. First, we studied the Donguibogam only; this is an encyclopedic narrative, and we did not review all classical texts. Second, because skincare-related terms were established by expert consensus, some subjectivity is inevitable. However, the experts sought to make objective judgments by consulting various references. Third, the functions of prescriptions featuring several herbs became those of single herbs. The proportions of individual herbs in prescriptions were not considered.

In summary, we used data mining to identify the characteristics of 52 medicinal herbs, by applying SRKs when analyzing the content of a classical medical text. Further in-depth experimental studies are needed, though our work reduces the time required for future experimentation and product development. Our results enhance the understanding of the previously unknown characteristics of medicinal herbs used for skincare and facilitate the discovering additional novel herbs.

Author contributions

Gayoung Cho: Conceptualization, Validation, Formal analysis, Writing - original draft. Hyo-Min Park: Methodology, Writing - original draft. Won-Mo Jung: Methodology, Software, Formal analysis, Visualization. Woong-Seok Cha: Methodology, Data curation. Donghun Lee: Validation, Investigation, Data curation, Writing - review & editing. Younbyoung Chae: Conceptualization, Investigation, Resources, Writing - review & editing, Supervision, Project administration, Funding acquisition.

Conflict of interest

The authors declare no conflict of interest.

Funding

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (No. 2018R1D1A1B07042313)

Ethical statement

This research did not involve any human or animal experiment.

Data availability

The data will be made available upon reasonable request.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.imr.2020.100436>.

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