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

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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, ointment 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 (Gunniera perpensa 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
candidate cognition-enhancing herbs,\textsuperscript{9,10} candidate anti-aging herbs,\textsuperscript{11} stroke treatments,\textsuperscript{12} and prescriptions for Parkinson-type rigidity.\textsuperscript{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.\textsuperscript{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 + 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

| 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, lusciousness, and substance | |
| 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 pelioma | |
| 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 | |
| 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 | Anti-aging |
| 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 | |
| 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 | Anti-inflammatory |
| 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 | |
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*) \(Z = 4.67\), 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*, *Cinnamomum 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 vulgare* L. (*Hordei Sclerotium*), *Cistanches Herba*, *Glycyrrhiza inflata* Benth. (*Glycyrrhizae Radix*), *Atractylodis Rhizoma* \(Z = 4.54\), *Astragali Radix* \(Z = 3.92\), *Ginseng Radix* \(Z = 3.14\), *Rehmanniae Radix* \(Z = 6.87\), *Honeysuckle Berries* \(Z = 6.47\), and *Dioscorea opposita* Thunb. (*Dioscoreae Rhizoma*).
vulgare L. (Hordei Fructus Germinatus) (Z = 4.94), stewing and concentrating material from *Equisetum arvense* L. (Asini Corii Colla) (Z = 5.42), seed of *Dolichos lablab* L. (Dolichoris Semen) (Z = 5.69), rhizome of *Acorus gramineus* Aiton (Acori Graminei Rhizoma) (Z = 6.44), flower of *Chrysanthemum indicum* L. (Chrysanthemi Flos) (Z = 6.89), fruit of *Anomum tsao-ko* Crevois & 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.”

**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.

**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), Schisandraceae 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)
Medicinal herbs related to anti-aging

Ten medicinal herbs were associated with anti-aging: Ginseng Radix (Z = 4.26), Rehmanniae Radix (Z = 3.63), tuberous root of Ophiopogon japonicus (Thunb.) Ker Gawl. (Liriope Tuber) (Z = 7.05), tuberous root of Asparagus cochinchinensis (Lour.) Merr. (Asparagus Tuber) (Z = 6.64), root of Lycium barbarum L. (Lycii Radicis Cortex) (Z = 5.25), fruit of Lycium barbarum L. or Lycium chinense Mill. (Lycii Fructus) (Z = 4.92), 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 & 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-inflammatory: rhizome of Cyperus rotundus L. (Cyperi 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 Rehd & E.H.Wilson (Magnoliae Cortex) (Z = 2.58), cortex of Cinnamomum cassia (L.) 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 amurensis Max. (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 Tsaoko Fructus (Z = 7.43).

Cyperi Rhizoma was associated with the term “exfoliate”; Piperis Longi Fructus with “deinsectization”; Atragradi 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 Tsaoko Fructus with “numbness.”

Medicinal herbs related to more than one skincare function

Of the 52 medicinal herbs, six were associated with two skincare functions: Schisandraceae Fructus with hydration and tonification, Massa Medicata Fermentata with whitening and tonification, Amomi Tsaoko 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 Radix Preparata, Aconiti Rhizoma, and the following herbs:

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    | Achyranthis Radix     | Tonification                    | Achyranthes bidentota polysaccharide (ABP) and Lycium barbarum polysaccharide (LB) inhibited nonenzymic glycation in a D-galactose-induced model of mouse aging; ABP was more effective than LB. |
| 2    | Aconiti Lateralis Radix Preparata | Tonification, Anti-inflammation | None.                                                                                             |
| 3    | Acori Graminei Rhizoma | Whitening                       | An Acorus gramineus extract inhibited tyrosinase activity and melanin synthesis.                    |
| 4    | Alpiniae Katsumadai Semen | Anti-inflammation              | An Alpinia katsumadai Hayata methanol extract reduced house dust mite-induced atopic dermatitis in NC/Nga mice. |
| 5    | Alpiniae Officinari Rhizoma | Tonification                   | An 80% (v/v) aqueous acetone extract from rhizomes of Alpinia officinarum inhibited melanogenesis in mice with theophylline-stimulated murine B16 melanomas. |
| 6    | Amomi Tsaoko Fructus  | Whitening                       | Catechins and catechol derivatives from the fruit of Amomum tsao-ko exhibited strong DPPH radical-scavenging and antioxidant activities. |
| 7    | Arisaematis Rhizoma   | Anti-inflammation               | None.                                                                                             |
| 8    | Asini Cori Colla      | Whitening                       | * Not an appropriate cosmetic ingredient (safety concerns).                                       |
| 9    | Asparagi Tuber        | Anti-Aging                      | None.                                                                                             |
| 10   | Astragali Radix       | Anti-inflammation               | An aqueous extract of Aasparagus cochinchinensis (Lour.) Merr. shoots exhibited strong radical-scavenging capacities in vivo and in vitro. |
| 11   | Atractylodis Rhizoma Alba | Tonification, Anti-inflammation | A compound from rhizomes of A. macrocephala inhibited NO production in a dose-dependent manner. |
| 12   | Cervi Parvum Cornu   | Tonification                    | A pharmacopuncture solution of Cervi Pantotrichum Cornu inhibited elastase activity and exhibited DPPH free radical-scavenging capacity. |
| 13   | Chrysanthemi Flos     | Whitening                       | Methanol and water extracts of Chrysanthemum indicum dose-dependently inhibited mushroom tyrosinase activity; the effects of the methanol extract were similar to those of kojic acid, a well-known tyrosinase inhibitor. |
| 14   | Cinnamomi Cortex      | Anti-inflammation               | Cinnamomum cassia bark that had undergone solid-state fermentation by Phellinus baumii reduced IL-31 expression in DNF-treated C57BL/6 mice. |
| 15   | Cinnamomi Ramulus     | Hydration                       | Cinnamomum cassia extract inhibited the development of atopic dermatitis-like skin lesions in NC/Nga mice by suppressing the T-helper 2 cell response. |
Table 3 (Continued)

| No. | Candidate herb          | Expected skin-related function | Reported skincare-related efficacy                                                                 |
|-----|-------------------------|--------------------------------|-----------------------------------------------------------------------------------------------------|
| 16  | Cistanches Herba        | Tonification                    | A phenylethanoid-rich extract from *Cistanche desertica* exhibited anti-fatigue activity.            |
| 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.                                                        |
| 18  | Curcuma longae Rhizoma  | Anti-inflammation               | A hot-water extract of *Curcuma longa* significantly inhibited UVB-induced increases in tumor necrosis |
|     |                         |                                | factor (TNF-α) and interleukin (IL-1β) at the mRNA and protein levels.                            |
| 19  | Cuscutae Semen          | Anti-Aging                      | An ethanol extract of *Cuscuta chinensis* exhibited antioxidant activity.                         |
| 20  | Cyperi Rhizoma          | Anti-inflammation               | Valencene (VAL) from *Cyperus rotundus* inhibited TNF-α/IFN-γ-induced activation of NF-κB.        |
| 21  | Dioscoreae Rhizoma      | Tonification                    | An extract of aerial bulblets of *Dioscorea japonica* Thumb inhibited NF-κB and MAPK signaling in RAW |
|     |                         |                                | 264.7 cells.                                                                                      |
| 22  | Dolichoris Semen        | Whitening                       | None.                                                                                              |
| 23  | Eucommiae Cortex       | Tonification                    | Pretreatment with aucubin from *Eucommia ulmoides* suppressed UVB-induced oxidative stress in the   |
|     |                         |                                | HaCat cell line.                                                                                    |
| 24  | Euphorbiae kansui Radix | Anti-Aging                      | *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.                                                                                     |
| 26  | Ginseng Radix           | Tonification                    | Panax ginseng C.A. Meyer root extract (PGRE) activated the human COL1A2 promoter in a concentration- |
|     |                         |                                | dependent manner.                                                                                   |
| 27  | Gypsum Fibrosum         | Anti-inflammation               | Byakko-ka-ninjin-to (BN) (a prescription composed of the root of *anemarrhena, ginseng, licorice, and rice*) |
|     |                         |                                | inhibited irishness in an NC mouse model of atopic dermatitis.                                     |
| 28  | Hoelen                  | Whitening                       | Hoelen significantly inhibited melanin synthesis via the inhibition of TRP-2 expression.            |
| 29  | Hordei Fructus Germinatus| Whitening                      | A compound isolated from young green barrel (*Hordeum vulgare* L.) inhibited melanin biosynthesis in B16 |
|     |                         |                                | melanoma cells.                                                                                    |
| 30  | Inulae Flos              | Whitening                       | Sesquiterpenes from *Inula britannica* inhibited melanin synthesis by suppressing tyrosinase expression via ERK and Akt signaling. |
| 31  | Jujubae Fructus         | Anti-inflammation               | An essential oil from *Zizyphus jujuba* inhibited skin inflammation in an animal model.          |
| 32  | Liriopis Tubi            | Anti-inflammation               | Application of 0.5% (w/v) retinol, bakuchiol, and *Ophiopogon japonica* root extract cream, and 30%  |
|     |                         |                                | (w/v) vitamin C improved skin firmness and reduced wrinkles and hyperpigmentation.                  |
| 33  | Lycii Fructus           | Anti-Aging                      | Mice consuming goji berry (Lycium barbarum) juice were protected from UV radiation-induced skin    |
|     |                         |                                | damage via an antioxidant pathway.                                                                 |
| 34  | Lycii Radics Cortex     | Anti-Aging                      | *Lycium barbarum* polysaccharide protected human keratinocytes against UVB-induced photo-damage.   |
| 35  | Magnoliae Cortex        | Anti-Aging                      | Magnoliae Cortex exerted an anti-inflammatory effect on *Porphyromonas gingivalis*-stimulated RAW 264.7 |
|     |                         |                                | cells.                                                                                              |
| 36  | Massa Medicata Fermentata| Whitening                      | *Triticum aestivum* L exerted protective effects in an experimental animal model of chronic fatigue |
|     |                         |                                | syndrome.                                                                                           |
| 37  | Morindae Radix          | Tonification                    | *Triticum aestivum* sprout extract attenuated 2.4-dinitrochlorobenzene-induced atopic dermatitis-like skin lesions in mice and chemokine expression in human keratinocytes. |
|     |                         |                                | A methanol extract of the roots of *Morinda officinalis* exhibited anti-fatigue effects in mice.      |
| 38  | Mume Fructus            | Anti-Aging                      | A *Prunus mume* extract exhibited a DPPH free radical-scavenging effect.                           |
| 39  | Nelumbinis Semen        | Anti-Aging                      | Nelumbo nucifera roots protected against UVB-induced wrinkle formation and loss of subcutaneous fat by |
|     |                         |                                | suppressing MCP3, IL-6, and IL-8 expression.                                                      |
| 40  | Osterici Radix          | Hydration                       | An aqueous extract of Rhizoma notopterygii inhibited contact sensitivity by decreasing cytokine localisation at the inflammation site; the extract also downregulated matrix metalloproteinase (MMP) activity. |
| 41  | Perillae Folium         | Anti-inflammation               | Luteolin from perilla (*Perilla frutescens* L.) inhibited the secretion of inflammatory cytokines including IL-1β and TNF-α from human mast cells. |
| 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.         |
| 43  | Piperis Longi Fructus   | Anti-inflammation               | *Piper longum* extract attenuated melanin production in melanoma B16 cells.                        |
| 44  | Plantagnis Semen        | Hydration                       | Plantamajoside from *Plantago asiatica* inhibited UVB- and advanced glycation end-products-induced   |
|     |                         |                                | MMP-1 expression by suppressing the MAPK and NF-κB pathways in HaCat cells.                       |
| 45  | Polygalae Radix         | Tonification                    | *Polygala tenuifolia* extract significantly inhibited HMC-1 cell degranulation and alleviated IMO     |
|     |                         |                                | stress-exacerbated atopic dermatitis symptoms by modulating the PKA/p38 MAPK signaling pathway.    |
| 46  | Polyperus               | Hydration                       | Polyperus exhibited anti-UV activity; this ranked second among 25 herbs evaluated.                 |
| 47  | Raphani Semen           | Anti-inflammation               | Compounds from *Raphanus sativus* seeds inhibited NO production in lipopolysaccharide-activated BV-2 cells. |
| 48  | Rehmanniae Radix        | Anti-Aging                      | Topical application of *Rehmannia glutinosa* extract inhibited mite allergen-induced atopic dermatitis in NC/Nga mice. |
| 49  | Schisandrae Fructus     | Hydration                       | Schisandrin from the fruit of *Schisandra chinensis* exhibited anti-inflammatory properties.        |
|     |                         |                                | Schisandrin and schisandrin B, the two major lignans of *Schisandra chinensis*, protected HaCat cells from UVB-induced cell death by antagonizing the UVB-mediated production of ROS and induction of DNA damage. |
| 50  | Scutellariae Radix      | Anti-inflammation               | A *Scutellaria baicalensis* 80% (v/v) ethanol extract exhibited anti-allergic effects on inflammationboth in vivo and in vitro. |
| 51  | Succinum                | Anti-inflammation               | None.                                                                                              |
| 52  | Zingiberis Rhizoma      | Tonification                    | A clinical trial enrolling 80 postmenopausal women showed that capsules containing 40 mg of *Tribulus terrestris*, 12.27 mg of *Zingiber officinale*, 3 mg of a *Crocus sativus* extract, and 11 mg of *Cinnamomum zeylanicum* improved menopausal symptoms. |
Asini Corii Colla, Dolichorh Semen, Euphorbiacee Kausi 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. Nineteen-seven candidate anti-aging herbs were identified through the data mining process, and 47 of those were selected for further analysis. Ten herbs listed in the Donguibogam have been used to treat Parkinson-like rigidity. Combinations of 13 herbs have been used to treat stroke. Additionally, 14 of 23 herbs that enhance cognition have been evaluated experimentally and clinically. 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 Radix and Lycii Fructus were reported to exert anti-aging effects. 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. Nelumbinis Semen exerts an anti-aging effect, and Nelumbo nucifera leaf protects against UBV-induced wrinkle formation. Only six herbs have not been recently evaluated in terms of skin effects: Aconiti Lateralis Radix Preparata, Arisaematis Rhizoma, Asini Corii Colla, Dolichorh Semen, Euphorbiaceae Kausi Radix, and Succinum. Notably, four of these (Aconiti Lateralis Radix Preparata, Arisaematis Rhizoma, Crotonis Semen, and Euphorbiaceae Kausi 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. Natural products exert their therapeutic effects by acting on multiple targets. A multi-component multi-target approach lies at the core of medicinal herb pharmacology. 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. An herbal formula is not just addition of individual herbs, and it can produce greater effect than the sum of its individual constituents. Toxicity of toxic ingredients can be reduced and new active compounds can be more effective by combination formulas. Under the paradigm of network pharmacology, combinations of multiple compounds can exert their therapeutic effects by acting on multiple targets. The most frequently used medicinal herb combinations can constitute a candidate group for the development of a new prescription for universal application. 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.

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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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