**Original Article** 

## **A** Brief Review on Polyherbal Antiaging Properties of *Panax Quinquifolius Linn*. And *Matricaria Chamomilla* for Skin Care

Patel Vaishnavi<sup>1\*</sup>, Dr. Shweta Paroha<sup>2</sup>, Pragnesh Patani<sup>3</sup>

<sup>1\*</sup>Department of Pharmacy, Khyati College of Pharmacy, Palodia, Ahmedabad.

<sup>2</sup>Associate Professor, Department of Pharmaceutics, Khyati College of Pharmacy, Palodia, Ahmedabad

<sup>3</sup>Principal and Professor, Department of Pharmacology, Khyati College of Pharmacy, Palodia, Ahmedabad

\*Corresponding Author: Patel Vaishnavi
\*Department of Pharmacy, Khyati College of Pharmacy, Palodia, Ahmedabad
Email: patelvaishu9429@gmail.com

#### **ABSTRACT:**

The quest for effective anti-aging skin care solutions has led to the exploration of natural remedies, among which polyherbal formulations combining ginseng and chamomile have garnered attention. This abstract presents a detailed overview of the anti-aging properties of ginseng and chamomile, two prominent herbal ingredients, when used in tandem for skin care. Ginseng renowned for its adaptogenic properties, contains active compounds such as ginsenosides that exhibit potent antioxidant effects. These compounds neutralize free radicals, thereby reducing oxidative stress, which is a major contributor to skin aging. Additionally, ginseng has been shown to enhance collagen synthesis, improve skin elasticity, and promote cellular regeneration, addressing common signs of aging such as fine lines and sagging. Chamomile on the other hand, is celebrated for its soothing and anti-inflammatory properties. Key constituents such as chamazulene and bisabolol contribute to its ability to calm irritated skin, reduce redness, and enhance skin barrier function. Chamomile also possesses antioxidant properties, which complement the effects of ginseng by further mitigating oxidative damage and supporting skin repair. When combined in a polyherbal formulation, ginseng and chamomile provide a synergistic effect that amplifies their individual benefits. The anti-aging potential of this combination is attributed to the interplay between ginseng's collagen-boosting and antioxidant properties and chamomile's anti-inflammatory and skin-soothing effects. This dual-action approach addresses multiple facets of skin aging, from reducing fine lines and improving skin texture to enhancing overall skin health and resilience. Clinical studies and empirical evidence supporting the efficacy of this polyherbal combination in skin care are emerging, though more research is warranted to fully understand the extent of their benefits. Nonetheless, the integration of ginseng and chamomile into skin care products represents a promising avenue for developing effective anti-aging treatments that harness the power of natural ingredients.

**KEYWORDS:** POLYHERBAL FORMULATIONS, GINSENOSIDES, APIGENIN, BISABOLOL, SYNERGISTIC EFFECTS, COLLAGEN SYNTHESIS, SKIN REPAIR.

#### INTRODUCTION:

Aging is characterized by the progressive loss of physiological function, which can result in either age-related diseases or geriatric syndromes; these include cardiovascular and obstructive pulmonary diseases, musculoskeletal disorders, a number of different cancer types, neurodegenerative diseases,

and skin disorders [1]. Intrinsic factors are determined by genetic and physiological changes, whereas extrinsic factors are promoted by external stimuli, such as ultraviolet radiation, diet, air pollution, abuse of tobacco and alcohol, lifestyle, toxins, and others [2]. Physiological changes to the skin: Thermoregulation, fluid balance, electrolytes and protein loss, production of vitamin D, waste clearance, sensation, immune function, and barrier function [3,4]. Scientific studies on chamomile have identified antioxidant, bactericidal, antidepressant, anti-inflammatory, anti-diabetic, antitumor, hepatoprotective, and antidiabetic activity [5,6]. Ginseng is popular in anti-aging skincare due to its potent antioxidant properties, which help protect the skin from oxidative stress and damage caused by free radicals. Its anti-inflammatory effects soothe irritation and redness, contributing to a more even complexion. Additionally, ginseng may stimulate collagen production, essential for maintaining skin's firmness and elasticity, and improve circulation, which delivers nutrients and oxygen to the skin for a radiant appearance. Furthermore, it aids in hydration by supporting the skin's barrier function and may enhance cell regeneration, helping to reduce age spots and uneven skin tone. Panax ginseng (Asian ginseng) has been utilized for centuries across various Eastern countries as both a medicinal herb and a functional food that supports health. Numerous studies have identified a range of pharmacological effects of ginseng on the immune, cardiovascular, endocrine, and central nervous systems [7]. Ginsenosides are the primary active compounds found in *Panax* ginseng. Although the root of Panax ginseng is traditionally regarded as the most significant part of the plant for medicinal use, with most research focusing on its ginsenosides, some studies have found that the leaves contain higher levels of ginsenosides compared to the root. Additionally, these studies have noted that PPD-type ginsenosides are more prevalent in the leaves than PPT-type ginsenosides. [8,9,10]. Chamomile, particularly its key components—apigenin and bisabolol—offers notable benefits for skincare. Apigenin exhibits anti-inflammatory and antioxidant properties, which help soothe irritated skin and protect against oxidative stress. Bisabolol, known for its anti-inflammatory and antimicrobial effects, enhances skin healing and reduces redness. Studies such as those by have shown chamomile's effectiveness in alleviating conditions like eczema and dermatitis, while its ability to improve skin hydration and texture has been documented by These properties make chamomile a valuable ingredient in skincare products designed to calm, protect, and rejuvenate the skin.



FIGURE: 01 Ginseng.

#### • GINSENG:

Kingdom : Plantae Order : Apiales

Class : Magnoliopsida Family : Araliaceae Genus : Panax L. Species: Panax ginseng.

CHEMICAL CONSTITUENT:

# Triterpenoid glycosides, commonly referred to as ginsenosides, are the primary active compounds in ginseng. Ginsenosides are categorized into two main groups: protopanaxadiols (PPD), which encompass Rb1, Rb2, Rg3, Rh2, Rc, Rd, and Rh3, and protopanaxatriols (PPT), which include Rg1, Rg2, Rh1, Re, and Rf. Additionally, ginseng contains other components such as saponins, polysaccharides, amino acids, volatile oils, and polyacetylenes [11,12].

1. Ginsenosides: Ginsenosides, also referred to as saponins, are the principal active components of ginseng. They are classified into various categories based on their chemical structures, such as: Protopanaxadiol (PPD) Ginsenosides: This category includes compounds like Rb1, Rb2, Rc, and Rd. These ginsenosides are recognized for their anti-inflammatory, antitumor, and neuroprotective effects [13]

Protopanaxatriol (PPT) Ginsenosides: This group encompasses compounds such as Re, Rf, and Rg1. They are linked to benefits including enhanced cognitive function, antioxidant activity, and improved sexual performance [14].

#### 2. Polysaccharides:

Ginseng contains complex carbohydrates known as polysaccharides, which exhibit immunomodulatory and antioxidant properties. Notable examples include Ginseng Polysaccharides (GPs) like G1, G2, and G3. These polysaccharides are believed to enhance immune function and mitigate oxidative stress [15].

#### 3. Phenolic Compounds:

Ginseng includes a range of phenolic compounds that contribute to its antioxidant effects. Among these are phenolic acids such as caffeic acid and ferulic acid, which are noted for their significant antioxidant and anti-inflammatory properties <sup>[16]</sup>.

#### 4. Essential Oils:

Ginseng also features essential oils that play a role in its aroma and therapeutic benefits. Key components, such as  $\beta$ -caryophyllene and  $\alpha$ -pinene, are associated with the plant's anti-anxiety and antidepressant effects [17].

#### **MECHANISM OF ACTION:**

**Skin elasticity/Collagen:** Ginseng can help the skin keep its smoothness by slowing the loss of collagen. "There are so many chemicals in ginseng root," It contains vitamin D & vitamin B12." All of this leads to enhanced oxygen circulation, as well as an increase in collagen formation in the dermis of skin [18].

**Antioxidant and blood circulation**: Ginseng also plays an antioxidant action via Nrf2 and increases the amounts of antioxidant enzymes including superoxide dismutase and glutathione peroxidase.

**Neuroprotection:** Modulation of the Akt and ERK 1/2 signalling pathways, repression of NF- $\kappa\kappa$ B, control of Ca2+ over influx, shielding against NO excess production, and decrease of the apoptosis-inducing factor <sup>[19]</sup>.

Groups	Contents		Ingredients
Saponin	Saponin (3–6%)	-	PPD ginsenosides
		-	PPT ginsenosides
		-	Oleanane ginsenosides
Non-saponin	N-containing substances (12–15%)	-	Proteins, amino acids
		-	Peptides, nucleic acids
		-	Alkaloids
	Fat-soluble components (1–2%)	-	Fat, fatty acids
		-	Essential oils
		-	Phytosterol
		-	Organic acids
		-	Phenolics
		-	Polyacetylenes
		-	Terpenes
	Carbohydrates (50–60%)	-	Polysaccharides
		-	Oligosaccharides
		-	Sugar, fiber, pectin
Others	Ash (4–6%)	-	Minerals
	Vitamin (0.05%)	-	Water-soluble vitamins

FIGURE: 02 Chemical Constituent of Korean ginseng

#### **USES:**

- Help in skin whitening
- Protect against pigmentation and photoaging
- Treat acne
- Reduce inflammation
- Helps in hydration boosting

#### **SIDE EFFECTS:**

• Skin rashes

#### **EXTRACTION METHOD:**

Extraction technologies are designed to maximize both the yield and quality of oil while keeping production costs low. Additionally, it is crucial that these technologies preserve the natural proportion of components present in the original material throughout the extraction process [18].

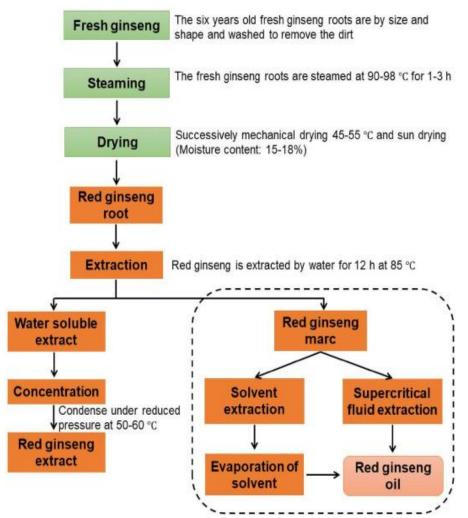


FIGURE: 03 Production methods for red ginseng extract and red ginseng oil.

#### TYPES OF EXTRACTION METHODS:

- 1. Conventional Extraction
- 2. Supercritical Fluid Extraction

#### 1. Conventional Extractions:

Solvent extraction is a traditional technique for producing plant oil, valued for its cost-effectiveness and high efficiency. Hexane is commonly utilized for RGO extraction because of its polarity [19.20]. However, hexane has only a moderate ability to extract both fatty acids and minor components from solid substances [21]. Other solvents, like petroleum ether, have been employed for extracting RGO, but their commercial use is limited due to their toxicity. A single solvent cannot extract all the desired components because red ginseng contains a wide range of lipid-soluble substances with varying polarities. Additionally, traditional methods such as hydro distillation and steam distillation can also be used to obtain red ginseng essential oil [22,23]. While traditional extraction methods are commercially viable and scalable, they have drawbacks, including being time-consuming, yielding lower amounts, losing valuable compounds, potentially contaminating with toxic solvent residues, and producing unwanted by-products [24].

#### 2. Supercritical Fluid Extractions:

Supercritical fluid extraction (SFE) offers an efficient alternative to traditional extraction methods. In SFE, red ginseng marc is placed in an extraction vessel, and a supercritical fluid is introduced at a controlled flow rate until optimal extraction conditions are reached. The supercritical solvent, now containing the dissolved materials, is then transferred to a separator where it is depressurized to collect the RGO, while the solvent can be recycled. Using CO2 as the solvent in SFE provides several benefits, including a low critical temperature, cost-effectiveness, non-toxicity, absence of Odor and taste, non-flammability, environmental friendliness, and ease of removing residues [25,26]. Moreover, supercritical CO2 fluid possesses advantageous solvent properties, as it quickly infiltrates solid matrices and efficiently dissolves a range of nonpolar and certain polar molecules [27]. Fermented ginseng seed oil extracted using supercritical CO2 fluid demonstrated notably higher levels of phenolic compounds and phytosterols compared to oil obtained through compression extraction or solvent extraction. Thus, supercritical CO2 extraction seems to be the most effective method for obtaining RGO [28].



FIGURE: 04 Red Ginseng Oil

#### CHAMOMILE:



FIGURE: 05 Chamomile.

Chamomile is valued in anti-aging skincare for its soothing and anti-inflammatory properties, which help calm irritated skin and reduce redness, giving the complexion a more even tone. Its

rich antioxidant content fights free radicals, which can cause premature aging and damage to skin cells. Additionally, chamomile supports skin hydration and can enhance the skin's barrier function, which is crucial for maintaining a plump, youthful appearance. Its ability to promote skin repair and reduce signs of stress contributes to a smoother and more resilient skin texture. It also has an antioxidant activity; botanical extracts have attracted great interest in the cosmetic and skin care area due to their rich composition and medicinal properties. *Matricaria chamomilla L*. extract is rich in flavonoids, terpenes, polysaccharides, among others, which may contribute for example anti-inflammatory and emollient effects to the formulation's bioactive properties [29,30,31].

#### **BIOACTIVE CONSTITUENTS:**

Chamomile contains various classes of bioactive compounds, which have been extracted and utilized in medicinal treatments and cosmetic products [32]. The plant contains 0.24-1.9% volatile oil, which is made up of various distinct oils. During steam distillation, the oil initially appears in colours ranging from bright blue to deep green, but it changes to dark yellow over time with storage. Despite this colour change, the oil retains its effectiveness. Around 120 secondary metabolites have been identified in chamomile, including 28 terpenoids and 36 flavonoids [33,34]. The essential oil from German chamomile flowers primarily contains the terpenoids α-bisabolol and azulenes, such as chamazulene and acetylene derivatives. Chamazulene and bisabolol are quite unstable and are best preserved in an alcoholic tincture. In contrast, the essential oil of Roman chamomile has lower levels of chamazulene and is primarily made up of esters from angelic and tiglic acids, along with farnesene and  $\alpha$ -pinene. Roman chamomile also contains up to 0.6% of sesquiterpene lactones of the germacranolide type, notably nobilin and 3-epinobilin. Major bioactive compounds across both types of chamomiles include α-bisabolol, bisabolol oxides A and B, chamazulene, farnesene, spiro-ether quiterpene lactones, glycosides, hydroxycoumarins, flavonoids (such as apigenin, luteolin, patuletin, and quercetin), coumarins (like herniarin and umbelliferon), terpenoids, and mucilage [35,36]. The flowers also contain several important phenolic compounds, chiefly flavonoids such as apigenin, quercetin, and patuletin, found as glucosides and various acetylated forms. Apigenin, in particular, stands out as the most significant flavonoid. Although it is present in only small amounts as free apigenin, it is mainly found as different glycoside forms [37-41].

#### **MODERN USES:**

1. Sleep and Insomnia:

Uses: Chamomile is commonly used for its gentle sedative properties to enhance sleep quality and relieve insomnia [42].

2. Digestive Health:

Uses: Chamomile is frequently used to ease digestive problems, including indigestion, bloating, and nausea [43].

3. Anxiety and Stress Reduction

Uses: Chamomile is employed for its soothing effects to assist in reducing anxiety and stress [44].

4. Skin Health:

Uses: Chamomile is applied topically or used in skincare products for its anti-inflammatory and soothing properties, helping with conditions like eczema and dermatitis [45].

5. Immune System Support

Use: Chamomile is thought to have immune-boosting properties and may assist in preventing common colds and infections [46].

#### TRADITIONAL USES:

Chamomile has been used for centuries in traditional medicine for its anti-inflammatory, antioxidant, mild astringent, and healing properties [47]. Traditionally, chamomile has been used to address a variety of conditions, including wounds, ulcers, eczema, gout, skin irritations, bruises, burns, canker sores,

neuralgia, sciatica, rheumatic pain, haemorrhoids, mastitis, and other health issues <sup>[48,49</sup>]. Externally, chamomile has been applied to treat diaper rash, cracked nipples, chicken pox, ear and eye infections, eye disorders such as blocked tear ducts and conjunctivitis, nasal inflammation, and poison ivy <sup>[50,51]</sup>.

Chamomile is commonly used to address skin and mucous membrane inflammations, as well as various bacterial infections affecting the skin, oral cavity, gums, and respiratory tract. An aqueous extract of chamomile is often utilized as a gentle sedative to soothe nerves, alleviate anxiety, and manage conditions such as hysteria, nightmares, insomnia, and other sleep disturbances [52].



FIGURE: 06 Chamomile.

FIGURE: 07 Chamomile oil

Chamomile has been appreciated for its digestive soothing properties and has been used to address a range of gastrointestinal issues, such as flatulence, indigestion, diarrhoea, loss of appetite, motion sickness, nausea, and vomiting [53,54]. Chamomile has been used to manage colic, croup, and fevers in children. In addition, it has been utilized as an emmenagogue and uterine tonic for women. It is also effective in relieving arthritis, back pain, bedsores, and stomach cramps [55].

#### **CHEMICAL CONSTITUENTS:**

Chamomile, notably \*Matricaria chamomilla\* (German chamomile) and \*Chamaemelum Nobile\* (Roman chamomile), is highly valued for its medicinal benefits. The therapeutic effects of chamomile are primarily due to its wide array of bioactive compounds.

- 1. Essential Oils: The essential oils of chamomile are integral to its therapeutic properties. Key components include:
- 1A. Bisabolol: Renowned for its anti-inflammatory and antimicrobial effects [56].
- 1B. Chamazulene: Provides anti-inflammatory and antioxidant effects [57].
- 2. Flavonoids: Chamomile is rich in various flavonoids that enhance its health benefits:
- 2A. Apigenin: A compound recognized for its anti-inflammatory and antioxidant properties [58].
- 2B. Luteolin: Known for its anti-cancer and anti-inflammatory properties [59].
- 3. Phenolic Compounds:

Chamomile features phenolic compounds that strengthen its therapeutic properties:

- 3A. Chlorogenic Acid: Delivers notable antioxidant and anti-inflammatory benefits [60].
- 3B. Caffeic Acid: Known for its antioxidant and anti-inflammatory activities [61].
- 4. Polysaccharides:

Chamomile includes polysaccharides that play a role in its immunomodulatory effects:

4A. Chamomile Polysaccharides: Compounds like inulin and pectin, which have demonstrated potential in enhancing immune function [62].

Flower

FIGURE: 08 Chamomile flower and its flavonoids apigenin structure.

#### **PROPERTIES:**

Chamomile, particularly its key components—apigenin and bisabolol—offers notable benefits for skincare. Apigenin exhibits anti-inflammatory and antioxidant properties, which help soothe irritated skin and protect against oxidative stress. Bisabolol, known for its anti-inflammatory and antimicrobial effects, enhances skin healing and reduces redness <sup>[63,64]</sup>. Studies such as those by have shown chamomile's effectiveness in alleviating conditions like eczema and dermatitis, while its ability to improve skin hydration and texture has been documented by these properties make chamomile a valuable ingredient in skincare products designed to calm, protect, and rejuvenate the skin <sup>[65]</sup>.

### POTENTIAL CONTRAINDICATIONS AND SAFETY CONCERNS ASSOCIATED WITH CHAMOMILE INCLUDE:

A relatively low percentage of people are sensitive to chamomile and develop allergic reactions people sensitive to ragweed and chrysanthemums or other members of the Compositae family are more prone to develop contact allergies to chamomile, particularly if they take other drugs that trigger the sensitization [66]. Between 1985 and 1991, a major clinical trial was carried out in Hamburg, Germany, to investigate how contact dermatitis develops from exposure to a mixture of substances derived from the Compositae family. During the study, twelve species from this family, including German chamomile, were tested separately whenever the mixture triggered allergic reactions [67]. Chamomile fell in the middle range (56.5%). A study involving 686 subjects exposed to either a sesquiterpene lactone mixture or a mixture of Compositae extracts led to allergic reactions in 4.5% of the subjects with conjunctivitis worsened their eye inflammation. However, drinking chamomile tea did not lead to any increase in eye inflammation [69].

#### **CONCLUSIONS:**

Combining ginseng and chamomile in skin care routines offers a powerful approach to combating signs of aging. Ginseng enhances skin vitality through its rich antioxidant content, which neutralizes free radicals and reduces oxidative stress. It also boosts collagen production, improving skin firmness and elasticity while alleviating inflammation to soothe irritated skin. Chamomile complements these effects with its own set of benefits, including anti-inflammatory properties that calm redness and irritation, as well as antioxidants that protect against environmental damage. Additionally, chamomile enhances skin hydration, which helps maintain elasticity and diminish the appearance of fine lines. Together, these herbs provide a holistic anti-aging solution, promoting a healthier, more youthful complexion by addressing both the structural and surface-level aspects of skin aging.

#### **REFERENCES:**

1. Li Z, Zhang Z, Ren Y, Wang Y, Fang J, Yue H, Ma S, Guan F. Aging and age-related diseases: from mechanisms to therapeutic strategies. Biogerontology. 2021;22(2):165-187.

- 2. Franceschi C, Garagnani P, Morsiani C, Conte M, Santoro A, Grignolio A, Monti D, Capri M, Salvioli S. The Continuum of Aging and Age-Related Diseases: Common Mechanisms but Different Rates. Front Med (Lausanne). 2018; 5:61.
- 3. Badro J, Côté AS, Brodholt JP. A seismologically consistent compositional model of Earth's core. Proc Natl Acad Sci U S A. 2014;111(21):7542-5.
- 4. Zouboulis CC, Ganceviciene R, Liakou AI, Theodoridis A, Elewa R, Makrantonaki E. Aesthetic aspects of skin aging, prevention, and local treatment. Clin Dermatol. 2019; 37(4):365-372.
- 5. Caverzan J, Mussi L, Sufi B, Padovani G, Nazato L, Camargo FB Junior, Magalhães WV, Di Stasi LC. A new Phyto cosmetic preparation from Thymus vulgaris stimulates adipogenesis and controls skin aging process: In vitro studies and topical effects in a double-blind placebo-controlled clinical trial. J Cosmet Dermatol. 2021; 20(7):2190-2202.
- 6. Sabouri-Rad S, Sabouri-Rad S, Sahebkar A, Tayarani-Najaran Z. Ginseng in Dermatology: A Review. Curr Pharm Des. 2017;23(11):1649-1666.
- 7. Di Blasio S, Shtrepi L, Puglisi GE, Astolfi A. A Cross-Sectional Survey on the Impact of Irrelevant Speech Noise on Annoyance, Mental Health and Well-being, Performance and Occupants' Behavior in Shared and Open-Plan Offices. Int J Environ Res Public Health. 2019;16(2):280.
- 8. Chen W, Balan P, Popovich DG. Analysis of Ginsenoside Content (*Panax ginseng*) from Different Regions. Molecules. 2019;24(19):3491.
- 9. Kang OJ, Kim JS. Comparison of Ginsenoside Contents in Different Parts of Korean Ginseng (*Panax ginseng* C.A. Meyer). Prev Nutr Food Sci. 2016;21(4):389-392.
- 10. Zhang, Y.-C.; Li, G.; Jiang, C.; Yang, B.; Yang, H.-J.; Xu, H.-Y.; Huang, L.-Q. Tissue-Specific Distribution of Ginsenosides in Different Aged Ginseng and Antioxidant Activity of Ginseng Leaf. *Molecules* 2014, 19, 17381-17399.
- 11. Kliner M, Keenan A, Sinclair D, Ghebrehewet S, Garner P. Influenza vaccination for healthcare workers in the UK: appraisal of systematic reviews and policy options. BMJ Open. 2016; 6(9).
- 12. Keen MA, Hassan I. Vitamin E in dermatology. Indian Dermatol Online J. 2016; 7(4):311-5.
- 13. Attele AS, Wu JA, Yuan CS. Ginseng pharmacology: multiple constituents and multiple actions. Biochem Pharmacol. 1999;58(11):1685-93.
- 14. Ratan ZA, Haidere MF, Hong YH, Park SH, Lee JO, Lee J, Cho JY. Pharmacological potential of ginseng and its major component ginsenosides. J Ginseng Res. 2021;45(2):199-210.
- 15. Tao R, Lu K, Zong G, Xia Y, Han H, Zhao Y, Wei Z, Lu Y. Ginseng polysaccharides: Potential antitumor agents. J Ginseng Res. 2023;47(1):9-22.
- 16. Yao F, Xue Q, Li K, Cao X, Sun L, Liu Y. Phenolic Compounds and Ginsenosides in Ginseng Shoots and Their Antioxidant and Anti-Inflammatory Capacities in LPS-Induced RAW264.7 Mouse Macrophages. Int J Mol Sci. 2019;20(12):2951.
- 17. Li, Y., Chen, W., & Liu, Y. Chemical composition and biological activity of ginseng essential oil. *Journal of Essential Oil Research*, 2012;24(5), 387-392.
- 18. A.C. Stratakos, A. Koidis Chapter 4 methods for extracting essential oils. Preedy VR Academic Press, editors, San Diego 2016, pp. 31-38.
- 19. M.R. Kang, H.M. Kim, J.S. Kang, K. Lee, S.D. Lee, D.H. Hyun, *et al.* Lipid-soluble ginseng extract induces apoptosis and G0/G1 cell cycle arrest in NCI-H460 human lung cancer cells Plant Foods Hum Nutr, 66 2011, pp. 101-106.
- 20. J. Yun, B.G. Kim, J.S. Kang, S.K. Park, K. Lee, D.H. Hyun, *et al.* Lipid-soluble ginseng extract inhibits invasion and metastasis of B16F10 melanoma cells J Med Food, 18 2015, pp. 102-108.
- 21. M.H. Lee, S.S. Kim, C.W. Cho, S.Y. Choi, G. In, K.T. Kim Quality and characteristics of ginseng seed oil treated using different extraction methods J Ginseng Res, 37 2013, pp. 468-474.
- 22. M. Khajeh, Y. Yamini, N. Bahramifar, F. Sefidkon, M. Reza Pirmoradei Comparison of essential oils compositions of *Ferula asafoetida* obtained by supercritical carbon dioxide extraction and hydro distillation methods Food Chem, 91 2005, pp. 639-644.

- 23. N. Yeddes, J.K. Chérif, A. Jrad, D. Barth, M. Trabelsi-Ayadi Supercritical SC-CO (2) and Soxhlet n-hexane extract of Tunisian *Opuntia Ficus indica* seeds and fatty acids analysis J Lipids, 2012; 914693-914693.
- 24. J.S. Choi, M.H. Jeon, W.S. Moon, J.N. Moon, E.J. Cheon, J.W. Kim, *et al. In vivo* hair growth-promoting effect of rice bran extract prepared by supercritical carbon dioxide fluid Biol Pharm Bull, 37 2014, pp. 44-53.
- 25. A.C. Stratakos, A. Koidis Chapter 4 methods for extracting essential oils. Preedy VR Academic Press, editors, San Diego 2016, pp. 31-38.
- 26. M. Zougagh, M. Valcárcel, A. Rios Supercritical fluid extraction: a critical review of its analytical usefulness Trends Anal Chem, 23 2004, pp. 399-405.
- 27. M. Khajeh, Y. Yamini, N. Bahramifar, F. Sefidkon, M. Reza Pirmoradei Comparison of essential oils compositions of *Ferula asafoetida* obtained by supercritical carbon dioxide extraction and hydro distillation methods Food Chem, 91 2005, pp. 639-644
- 28. M.H. Lee, Y.K. Rhee, S.Y. Choi, C.W. Cho, H.D. Hong, K.T. Kim Quality and characteristics of fermented ginseng seed oil based on bacterial strain and extraction method J Ginseng Res, 41 2017, pp. 428-433
- 29. Bedi MK, Shenefelt PD. Herbal therapy dermatology. Arch Dermatol 2002; 138; 232-242.
- 30. Aburjai T, Natsheh FM. Plants used in cosmetics. Phytotherapy Res 2003; 17: 987-1000.
- 31. Baumann LS. Less-known botanical cosmeceuticals. Dermatol Ther 2007; 20: 330-342.
- 32. Der MA and Liberti L: Natural Product Medicine: A Scientific Guide to Foods, Drugs, Cosmetics. George F. Stickley Co., Philadelphia, 1988.
- 33. Darker CD, Nicolson GH, Carroll A, Barry JM. The barriers and facilitators to the implementation of National Clinical Programmes in Ireland: using the MRC framework for process evaluations. BMC Health SERV Res. 2018;18(1):733.
- 34. McKay DL and Blumberg JB: A review of the bioactivity and potential health benefits of chamomile tea (Matricaria recutita L.). Phytother Res 20: 2000 519-530.
- 35. Lemberkovics E, Kéry A, Marczal G, Simándi B and Szöke E: Phytochemical evaluation of essential oils, medicinal plants and their preparations. Acta Pharm Hung 68: 1998 141-149.
- 36. Baser KH, Demirci B, is can G, et al: The essential oil constituent and antimicrobial activity of Anthemis aciphylla BOISS. Var. discoidea BOISS. Chem Pharm Bull 54: 2006; 222-225.
- 37. Babenko NA and Shakhova EG: Effects of Chamomilla recutita flavonoids on age-related liver sphingolipid turnover in rats. Exp Gerontol 41: 32-39, 2006; 15.
- 38. Redaelli C, Formentini L and Santaniello E: Reversed-phase high-performance liquid chromatography analysis of apigenin and its glucosides in flowers of Matricaria chamomilla and chamomile extracts. Planta Med 42: 288-292, 1981; 16.
- 39. Avallone R, Zanoli P, Puia G, Kleinschnitz M, Schreier P and Baraldi M: Pharmacological profile of apigenin, a flavonoid isolated from Matricaria chamomilla. Biochem Pharmacol 59: 1387-1394, 2000; 17.
- 40. Svehliková V, Bennett RN, Mellon FA, et al: Isolation, identification and stability of acylated derivatives of apigenin 7-O-glucoside from chamomile (Chamomilla recutita [L.] Rauschert). Phytochemistry 65: 2323-2332, 2004; 18.
- 41. Srivastava JK and Gupta S: Antiproliferative and apoptotic effects of chamomile extract in various human cancer cells. J Agric Food Chem 55: 2007; 9470-9478.
- 42. A study in *The Journal of Clinical Sleep Medicine* found that chamomile extract significantly improved sleep quality and reduced symptoms of insomnia in older adults 2023.
- 43. An article in *Phytotherapy Research* reported that chamomile tea effectively reduced symptoms of gastrointestinal discomfort and improved overall digestive health 2022.
- 44. A review published in *The American Journal of Clinical Nutrition* reviewed evidence showing that chamomile supplementation can help decrease anxiety levels and improve mood 2021.
- 45. A study in *Journal of Cosmetic Dermatology* found that chamomile extract was effective in reducing inflammation and irritation in patients with eczema 2022.

- 46. A research article in *Journal of Herbal Medicine* highlighted that chamomile had a notable effect on enhancing immune response and reducing the incidence of common colds 2023.
- 47. Rocha LA, Gomes ED, Afonso JL, Granja S, Baltazar F, Silva NA, Shoichet MS, Sousa RA, Learmonth DA, Salgado AJ. *In vitro* Evaluation of ASCs and HUVECs Co-cultures in 3D Biodegradable Hydrogels on Neurite Outgrowth and Vascular Organization. Front Cell Dev Biol. 2020; 8:489.
- 48. DeLeo PC, Huynh C, Pattanayek M, Schmid KC, Pechacek N. Assessment of ecological hazards and environmental fate of disinfectant quaternary ammonium compounds. Ecotoxicol Environ Saf. 2020; 206:111116.
- 49. Awang DVC: Tyler's Herbs of Choice: The Therapeutic Use of Phytomedicinal. Taylor and Francis Group, CRC Press, New York, 2006.
- 50. Muir WW, Ueyama Y, Noel-Morgan J, Kilborne A, Page J. A Systematic Review of the Quality of IV Fluid Therapy in Veterinary Medicine. Front Vet Sci. 2017; 4:127.
- 51. Rocha LA, Gomes ED, Afonso JL, Granja S, Baltazar F, Silva NA, Shoichet MS, Sousa RA, Learmonth DA, Salgado AJ. *In vitro* Evaluation of ASCs and HUVECs Co-cultures in 3D Biodegradable Hydrogels on Neurite Outgrowth and Vascular Organization. Front Cell Dev Biol. 2020; 8:489.
- 52. Forster HB, Niklas H and Lutz S: Antispasmodic effects of some medicinal plants. Planta Med 40: 1980; 309-319.
- 53. Rocha LA, Gomes ED, Afonso JL, Granja S, Baltazar F, Silva NA, Shoichet MS, Sousa RA, Learmonth DA, Salgado AJ. *In vitro* Evaluation of ASCs and HUVECs Co-cultures in 3D Biodegradable Hydrogels on Neurite Outgrowth and Vascular Organization. Front Cell Dev Biol. 2020; 8:489.
- 54. Sakai H and Misawa M: Effect of sodium azulene sulfonate on capsaicin-induced pharyngitis in rats. Basic Clin Pharmacol Toxicol 96: 2005; 54-55.
- 55. Peña D, Montes de Oca N and Rojas S: Anti-inflammatory and anti-diarrheic activity of Isocarpha cubana Blake. Pharmacol Online 3: 2006; 744-749.
- 56. Taboada, A., & Rodríguez-Gómez, J. Essential oil of chamomile: Chemical composition and biological activities. *Journal of Essential Oil Research*, 17(2), 2005; 169-174.
- 57. Basch, E., Ulbricht, C., Kuo, G., & Galik, J. Chamomile: An herbal medicine of the past with a bright future. *Modern Research in Medical Herbalism*, 1(1), 2004; 27-33.
- 58. Dastmalchi, K., & Moghaddam, H. Flavonoids in chamomile: Chemistry and health effects. *Phytotherapy Research*, 21(2), 2007; 105-112.
- 59. Denizot AL, Besson V, Correra RM, Mazzola A, Lopes I, Courbard JR, Marazzi G, Sassoon DA. A Novel Mutant Allele of Pw1/Peg3 Does Not Affect Maternal Behavior or Nursing Behavior. PLoS Genet. 2016;12(5)
- 60. Kroll, J., & Kroll, P. Chlorogenic acid in chamomile: Health benefits and therapeutic potential. *Journal of Agricultural and Food Chemistry*, 52(8), 2004; 2210-2215.
- 61. Beutler, J. A., & Agbaria, R. Chamomile's caffeic acid and its role in health benefits. *Journal of Herbal Medicine*, 15(3), 2005; 265-273.
- 62. Fuchs, A., & Zieger, M. Polysaccharides in chamomile: Effects on immune response. *Carbohydrate Polymers*, 89(4), 2012; 852-860.
- 63. Qi R, Geng X, Huang B, Chen Y, Jiang H, Zou Y, Wang W, Li Y, Li Y, Yin L, Liu A, Yang X, Li J, Yu H. Outcomes of STN-DBS in PD Patients with Different Rates of Disease Progression Over One Year of Follow-Up. Front Neurol. 2020; 11:600.
- 64. Rocha LA, Gomes ED, Afonso JL, Granja S, Baltazar F, Silva NA, Shoichet MS, Sousa RA, Learmonth DA, Salgado AJ. *In vitro* Evaluation of ASCs and HUVECs Co-cultures in 3D Biodegradable Hydrogels on Neurite Outgrowth and Vascular Organization. Front Cell Dev Biol. 2020: 8:489.
- 65. Muir WW, Ueyama Y, Noel-Morgan J, Kilborne A, Page J. A Systematic Review of the Quality of IV Fluid Therapy in Veterinary Medicine. Front Vet Sci. 2017; 4:127.

- 66. Budzinski JW, Foster BC, Vandenhoek S and Arnason JT: An in vitro evaluation of human cytochrome P450 3A4 inhibition by selected commercial herbal extracts and tinctures. Phytomedicine 7: 2000; 273-282.
- 67. Hausen BM: A 6-year experience with a Compositae mix. Am J Contact Dermat 7: 1996; 94-99.
- 68. Paulsen E, Andersen KE and Hausen BM: Compositate dermatitis in a Danish dermatology department in one year (I). Results of routine patch testing with the sesquiterpene lactone mix supplemented with aimed patch testing with extracts and sesquiterpene lactones of Compositate plants. Contact Dermatitis 29: 1993; 6-10.
- 69. Subiza J, Subiza JL, Alonso M, Hinojosa M, Garcia R, Jerez M and Subiza E: Allergic conjunctivitis to chamomile tea. Ann Allergy 65: 1990; 127-132.