

REVIEW

Medicinal Plants Meeting With Mud: Phyto-Peloid

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Abstract

For thousands of years, human beings have used various healing waters, plants, and muds from nature for health and beauty purposes. Nature and return to natural which we observe too often in the world today, has also increased the use of natural products. The use of certain muds for medical purposes is called peloidotherapy.

These subterranean and marine originated materials, which we named as mud, formed by various organic and inorganic substances in geological layers for thousands of years. Today, they are used for health and cosmetic purposes following the characteristics of organic and inorganic substances in their content, which vary according to their geography.

Studies show that; in the cures performed with the addition of peloidotherapy, the number of inflamed joints and the number of painful joints and pain severity decreased significantly ($p < 0.001$), joint function and quality of life significantly increased ($p < 0.05$), and symptoms of rash and itching ($p < 0.05$) decreased as.

As a new approach today; the use of muds obtained by combining medicinal plants widely used in the world for medical and cosmetic purposes is called phyto-peloid treatment. Considering the widespread and various medical mud resources and medicinal plant resources of our country, it is possible to be in the leading position in this regard.

The purpose of our research is to make difference about this value existing in our country, to make determinations and offer solutions on the existing applications and deficiencies in the mud existence and usage areas of our country, by taking into consideration the studies and applications made in the world.

Keywords: Mud, Medicinal Plants, Health, Cosmetics, Antimicrobial

INTRODUCTION

Mud has been used for thousands of years for both treatment and beauty. The beneficial properties of the mud, which is formed by the decay of biological substances, minerals, plant and animal residues for thousands of years, depends on humic substances. These substances such as temperature, content, mechanical which have different effects, are naturally used in the form of mud (peloid) applications. It is a miracle of nature that cleans and repairs the skin, supports the body with the minerals it contains, brings vitality and health, and reduces stress¹. For this purpose, local and foreign literature and websites have been examined and the data about the usage areas of humic substances in thermal tourism have been evaluated. Peloids are a mixture of inorganic and organic substances for thousands of years as a result of biological and geological effects. There are

different applications in the form of whole body, local application or packages for both treatment and cosmetic purposes². The effects of mud treatment are similar to those of treatments with thermo-mineral waters. Depending on the content and physical-chemical differences, muds are used in treatment with their thermal, mechanical and chemical effects. They react in the form of a compliance therapy by stimulating the hypothalamohypophyseal axis³.

Anatolian lands are the cradle of civilization. When Anatolian history is analyzed, the use of thermo-mineral water, which started in Roman baths in its best-known form, has become widespread in Seljuks and Ottomans and became known worldwide. These waters and muds have been used for health and beauty in these lands for thousands of years⁴.

DEFINITION OF PELOID

Peloides are defined as “organic and/or inorganic substances originating from subterranean and sea caused by natural geological and/or biological events”. It contains organic materials such as bacteria, algae, diatoms, protozoa, gastropods, as well as healing minerals such as sulfur, iodine, salt, and healing mixtures of inorganic minerals such as clay, quartz, calcite; it is rich in minerals such as magnesium, sodium, calcium, and potassium, which are important in the structure and normal function of our body⁵. Also, cyanobacteria, green algae, and diatoms are gradually colonized and this ensures that peloids have a microbiota. This microbiota generally consists of thermophilic microorganisms^{6,7}.

Peloids are diversified as follows:

- Peat: High water binding capacity, acid pH peloids. These muds are containing various natural dyes, humic acids and estrogen-like molecules that can be absorbed from the skin.
- Turbas: They are small-grained sediments that settle in still waters. Mineral marshes are formed in environments where thermo-mineral waters originate.
- Marine and Delta Slime: These are inorganic sediments that settle in sea and river deltas.
- Soils: Outside the water communities, they are powdered sediments formed by the crumbling, breaking down and decomposition of rocks or organic matter⁸.

The mechanism of action of peloids:

As a thermal feature, there is heat conduction from pellets to particles, molecules to molecules in the form of condensation in the peloid, and convection in water immersion. Peloids mixed with a predetermined amount of thermo-mineralized water or tap water before to use for appropriate density and temperature. Peloid has a high heat holding capacity, therefore it retains heat for a long time. The skin and peloid temperature are equalized by the heat provided by the peloid layer during direct skin contact. Peloid stores heat for a long time and releases it slowly to the area it is applied to. Heat penetrates deep into the body and gradually begins to decrease. For

treatment, they are applied to certain body areas in the form of full baths, local wraps, and packs⁹.

Peloids are available in different particle sizes in nature that can be made into small particles when necessary. Peloids have high heat capacities, slow transmissions, and can be applied for a longer time at higher temperatures compared to mineral waters. Full, half-peloid baths are applied at 39-40 ° C for 15-20 minutes. In cases where full bath application cannot be performed, the application can be done in the form of sitting and limb baths at a temperature up to 50 ° C. Generally, it is done in total of 15-18 applications in a cure every day or 2-3 days intervals. As a special cure, vaginal and rectal applications are performed at 45-52 ° C in the form of 20 cycles, once a day for 15-20 minutes¹⁰.

After the application period is over, the patient takes a warm shower and cleans the mud on his body. It is appropriate to rest up to 1 hour depending on the patient's condition. This cure application is applied in locomotor system diseases, rheumatic diseases, trauma or post-operative care and rehabilitation, skin diseases, gynecological diseases, and some digestive and urogenital diseases as a result of the examination, depending on the diagnosis and decision of the related physician. Due to its anti-inflammatory effect, it is preferred for infections with different localization of the genital area. Local and general hyperthermia, which occurs with increased blood supply and circulation, helps resorption of the infection. Due to its effect on increasing blood circulation, it stimulates follicles in ovarian failure, increases hormonal activities and regulates its cycle.

Peat, which is also characterized as swamp mud, contains a high rate of estrogen, especially humic acid at acid pH, with high water binding capacity. Another known effect is the stimulating effect on the hypothalamic, pituitary-adrenal system. It is recommended for primary and secondary hypoplasias of the uterus, hypo-hypermenorrhea, amenorrhea, monophasic cycle, corpus luteum insufficiency, and treatment. It is known that



especially in the treatment of infertility, satisfactory results are obtained with local or package applications³.

The mechanism of action of peloids is not limited only to their thermal effects. There is a microbiota that constitutes its content and this microbiota may have antimicrobial, anti-inflammatory properties for pathogenic species⁷. In this way, it can also be used as a therapeutic agent for lesioned skin. Although the microbiota possessed by peloids is thought to be enriched by active compounds with various metabolic products, the development of microorganisms on peloids has not been studied in detail. Studies for peloids generally focus on their chemical composition and the biological mechanism of their effects¹¹.

Peloidotherapy is still used in hospitals affiliated to the Ministry of Health. On the website of Konya Training and Research Hospital, section of peloidotherapy indicates that natural mud has pain relieving, antioxidant, cell regenerating and skin tightening effects. Peloidotherapy is actively applied in 4 hospitals of the Ministry of Health, especially in the locomotor system and skin diseases¹².

THE USE OF MUD IN THE FIELD OF HEALTH AND COSMETICS

There are dozens of published studies on the use of mud in the treatment of various diseases in the field of evidence-based medicine worldwide.

In a study conducted by Barassi et al., there are 63 patients with neuromuscular disorders, they showed that kinesiotherapy and mud treatment, which was applied 5 days a week for 2 weeks, was effective in relieving patients' quality of life and physical disability¹³.

In a study by Angioni et al., 66 patients with chronic low back pain due to osteoarthritis were discussed. Local mud treatment and thermo-mineralized water bath were applied to these patients for 2 weeks, and only drug treatment was given to the control group. In the patient group who underwent mud therapy, at the beginning of the study, 2nd week and 12th week blood tests

were done and the protein levels in the blood were determined.

Accordingly after mud treatment ($\geq 2,5$ fold), inhibin beta A subunit (INHBA), activin A receptor type 2B (ACVR2B), angiopoietin-1 (ANGPT1), beta-2-microglobulin (B2M), growth differentiation factor 10 (GDF10), C-X-C motif chemokine ligand 5 (CXCL5), fibroblast growth factor 2 (FGF2), fibroblast growth factor 12 (FGF12), oxidized low density lipoprotein receptor 1 (OLR1), matrix metalloproteinase 13 (MMP13) significantly increased. On the other hand (≤ 0.65 fold), Apolipoprotein C-III (ApoC3), interleukin 23 alpha subunit p19 (IL23A) and syndecan-1 (SDC1) proteins were also found to have a significant decrease. There was a significant clinical improvement in pain score, quality of life, and joint limitation¹⁴.

In a randomized controlled single-blind study by Varzaityte et al., stage III. changes in joint functions after balneotherapy and mud treatment of patients with knee osteoarthritis were investigated. Thermo-mineralized water bath and local mud were applied 10 times for 1 month, and a significant improvement in joint functions, joint pain, and joint stiffness was detected after 1 month¹⁵.

Min KJ et al. investigated the effect of short term thermo-mineralized water and mud treatment on patients with chronic hip pain. As a result, short term application of thermo-mineralized water and mud is significantly beneficial in patients with chronic hip pain. It is an important study in terms of understanding that patients who have short term breaks and who think that long term benefits can be provided in spa treatments are short in their treatments¹⁶.

In a double-blind randomized controlled study by Kiraly et al., 60 patients with knee osteoarthritis were divided into 2 groups. Both groups received 10 times mud treatment from 2 different regions for 2 weeks. In the determination made at the end of the study and after 12 weeks, there was a significant ($p < 0.05$) improvement in pain, joint function, and quality of life in both groups¹⁷.



In the study conducted by Cozzi et al. in Italy, the effects of mud treatment in seronegative spondylarthritis were investigated. In enteropathic spondylarthritis, it has been found that there is a significant improvement in bowel symptoms without worsening. It is also shown that ankylosing spondylitis is clinically improved with long term especially cutaneous lesions, joint function, psoriatic arthritis¹⁸.

The use of mud, which is used extensively in locomotor system diseases, is also common for the treatment, care and cosmetic purposes of skin diseases. It has numerous benefits for the skin. Some of these are to remove acne and remove blackheads. It also has the feature of removing skin blemishes that occur during pregnancy or from the sun. It softens and revitalizes the skin since it prevents blood collection. It cleans the dead skin and makes the skin smooth by exfoliation. It has been proven to benefit diseases such as psoriasis and eczema. It has the anti-aging effect that combats wrinkles with its antioxidant feature. It makes detox by absorbing the toxins and harmful substances from the body and removing them from the body. It is effective against cellulite, relaxes the body, relieves fatigue, and inflammation¹. It has been stated that mud application is also actively used in the treatment of seborrheic dermatitis in the article of Borda et al¹⁹.

The physical and chemical response of the skin was investigated in the short-term application of Hamed and his friends with Dead Sea mud on normal people's skin. The moisture of the skin, transepidermal water loss, erythema, and melanin levels and ph values of the skin were checked at 30th and 60th minutes after mud application. Accordingly, it has been observed that mud application increases the moistening of the skin and does not harm barrier resistance, ph and melanin-erythema levels²⁰.

The efficacy of mud therapy in psoriatic arthritis patients treated with TNF inhibitors (Tumor necrosis factor) has been investigated by Cozzi et al. There are 36 patients treated with TNF inhibitors for the last 6 months were divided into 2

randomized groups of 18. In the first group, in addition to drug treatment, 12 mud packs and 12 thermo-mineralized water treatments were applied, and the other 18 patients continued to receive drug treatment only. In patients, parameters such as sensitive and swollen joints, VAS (Visual Analog Scale) scrub, SF (Short Form)-36 scrub and blood CRP were monitored for 45 days. As a result, significant improvements were detected in PASI ($p < 0.005$), DAS28 ($p < 0.05$), and HAQ ($p < 0.001$) parameters between Day 1 and Day 45 in the mud treatment group. These data demonstrate a marked improvement in joint and skin inflammation and clinical findings in patients treated with mud and thermo-mineral water²¹.

Clinical studies conducted by Riyaz et al. reveal the benefits of using mud in psoriasis, atopic dermatitis, vitiligo and many other types of dermatitis²².

Constantino et al. conducted a study on 30 patients with psoriasis disease. 19 Male and 11 female patients were randomly divided into 2 groups. Group 1 received mud and thermo-mineralized bath treatment for 12 days, and group 2 received medication only. As a result, it was found that rash and itching symptoms were significantly decreased in the same ratio ($p < 0.05$) in both groups. In this case, the researchers concluded that mud and bath treatment in psoriasis disease has the same value as drug treatment²³.

Carabelli et al. performed thermal mud applications on normal, dry and seborrheic skin and evaluated the results after 14 days of treatment. Accordingly, it was found that cutaneous ph and sebum level improved in seborrheic skins applied with thermal mud²⁴.

THERAPEUTIC AND COSMETIC USE OF CERTAIN PLANTS

Plants in other words herbs have been used in medicine for thousands of years. Physicians have used many different plants in the treatment of diseases since ancient times. The first accepted medical botanist Dioscorides (AD 40-90)



represented more than a hundred medicinal plants in his well-known book *De Materia Medica*. He also explained the use of these plants and approximately six hundred herbal drugs. We provide some of our important drugs from plants. For instance, one of the most common antipyretic drugs aspirin is a semi-synthetic drug made from willow bark. Several examples like these have lead to medical practice today to treatment diseases and improve health.

Osteoarthritis is one of the most prevalent chronic joint inflammatory disease in the world. It is mainly affecting significant joint replacements such as the hips, knees, and hands²⁵ progressing chronic pain, disability, and occasionally swelling in the joints. Research indicates that patients with osteoarthritis prefer complementary alternative medications to conventional drug medications²⁶. Various plants have been used for a long time with traditional knowledge for treatments of inflammatory arthritic conditions. In a study reviewed by Dragos et al. shows that topical usage of certain plants such as *Arnica montana*, *Boswellia spp.*, *Symphytum officinalis*, and *Zingiber officinalis* improving the life quality and reducing the pain²⁷.

Besides joint diseases, herbs are commonly used for skin problems like acne, alopecia, bacterial and fungal infections of skin, chronic venous insufficiency, dermatitis, herpes simplex, herpes zoster, hyperhidrosis, pruritus, psoriasis, wounds and burns²⁸. They are also applied for skin care purposes apart from diseases. These herbal remedies are applied topically in different forms, for instance, dried extracts, creams, ointment, solutions and wet-wrap dressings²⁹. Herbal products consist of various compounds with different properties in comparison to isolated compounds. Some of these compounds of herbal medicine can act primarily as antimicrobials, others can serve as antioxidants, some may have anti-inflammatory functions and the rest of them can still maintain healing properties³⁰.

According to the data from the Ministry of Economy, Turkey; most of the multinational companies operating in the cosmetics industry

engage in the production and marketing activities in Turkey. Many foreign investors in the sector produce through license agreements and joint ventures. Depending on economic developments in Turkey, cosmetics and personal care products market has grown an average of 10% each year. It is estimated that the share of natural cosmetics and personal care products in the market is around 5%. This situation is in parallel with the world market. Only 10% of products marketed in Turkey are products originating in Turkey.

Hair care products have the biggest share among the sector products. Shampoos constitute about 59% of hair care products. Shaving products, depilators, bath and shower products, especially hand soaps, lip and eye make-up materials, deodorants and antiperspirant products, perfumes, colognes and baby care products are the main products.

In our country, natural soaps, shampoos, other hair care products and hair dyes, skin care products, body care products and other natural cosmetics have started to be produced in the sector in recent years. Especially natural soap and shampoo production is carried out by many small scale companies across the country. The world-famous laurel and olive oil soaps are produced in large quantities in Turkey. Some of the companies producing cosmetics also develop products with natural additives. In the cosmetic products category, approximately 170,000 products, 46,000 of which are local, are distributed in the local market. The number of companies in the sector registered in the electronic notification system of the Ministry of Health is 3,250 and 14,000 people are employed in these companies. In addition to large firms in the market, many small and medium sized firms that produce natural, organic and natural additive products also operate³¹.

Republic of Turkey Ministry of National Education Ministry of Education Beauty and Hair Care Services Basic Cosmetics 815sbg003 Megep training;

Cosmetics are as old as human history. Since the ages, humans have treated their diseases with

plants, water or mud, discovered the benefits of spring waters, burned incense to repel evil spirits, sometimes painted their faces and bodies with earth dyes to impress their gods, sometimes frighten their enemies. As well as men are painted to impress their enemies, women are also painted to decorate. The best example of this in history is the Egyptian queen Cleopatra. Cleopatra applied not only make-up but also exfoliation applications with Nile sand, entered the beauty baths with milk and applied masks with various herbal mixes, rubbed her body with essences and perfumed after the mud bath. Clay in the form of clay has been used by humans for medicine for thousands of years as it has all the richness of the earth. Today, as it was in the past, it is continued to use the active substances by entering directly into mud baths, and it is continued to be used by taking the valuable substances of the mud or by adding them to oily skin care products and body thinning care products³².

POSSIBLE USE OF HERBAL MUD AS AN ANTIMICROBIAL/ANTIVIRAL AGENT

Although the microbiota contained by the mud gives it some microbiological active properties, it has not been studied enough. On the other hand, many medicinal plants have antibacterial, antifungal and antiviral actions. *Mentha piperita*, *Thymus vulgaris*, *Hydrastis Canadensis*, *Berberis vulgaris*, *Urtica dioica*, *Curcuma longa*, *Zingiber officinale* are among the commonly used medicinal plants as infusion or tincture³³. This kind of plants are especially used in the treatment of infectious diseases today. Because in recent years, antimicrobial agent resistance has increased considerably, and besides, causes such as treatment costs, negative side effects of antibiotics/drugs have required low-toxic, easily accessible supportive or therapeutic natural products. *Glycyrrhiza glabra*, *Cistus creticus*, and *Sambucus nigra* plants stand out due to their antiviral properties. It is sold commercially in forms such as syrup and pastille^{33,34}.

Medicinal plants can show their antimicrobial effects not only systemically but also locally in

topical applications. Various extracts or creams from *Panax ginseng*, *Calendula officinalis*, *Arnica montana*, *Aloe vera*, *Vitis vinifera seed*, *Angelica sinensis*, *Ananas comosus*, *Symphytum officinale*, *Glycyrrhiza glabra*, *Hypericum perforatum*, *Momordica charantia* plants are used topically. Studies have shown that these medicinal plants have anti-inflammatory, antimicrobial, itch relief, and soothing effects, and proliferative properties on epidermis cells. Accordingly, they have topical use in wound treatment. In some studies, it has been determined that extracts obtained from *Panax ginseng*, *Calendula officinalis*, *Arnica montana* plants have anti-inflammatory and antimicrobial properties and have a wound-healing effect in vitro and in vivo testings^{35,36,37}.

Aloe vera has been shown to improve eczema lesions on animal and human studies and to reduce *Staphylococcus aureus* colonization, and IgE levels^{38, 39, 40}. Theodaris (2017) found in his double-blind randomized controlled study that medicinal plant containing cream significantly reduced psoriasis and eczema lesions⁴¹. Cream made from *Rheum palmatum* root extract (Chinese rhubarb), *Scutellaria baicalensis* root extract (Chinese skullcap), *Cnidium monnieri* fruit extract (Monnier's snow parsley), *Glycyrrhiza glabra* (licorice) has been shown to reduce atopic dermatitis lesions in open-labelled self-controlled clinical research⁴². It has been shown in vitro that olive oil and propolis have antiviral activity on Herpes viruses that cause shingles and herpes⁴³. Lip cream made from propolis extract has been shown to provide significant results for herpes treatment in a double-blind randomized controlled trial⁴⁴.

Considering all of these, the use of Traditional and Complementary Medicine applications in dermal treatments is gradually increasing^{45, 46}. There are many creams and oil essences on the market used in the treatment of dermatological problems such as psoriasis, eczema, wounds, herpes, and skin inflammation^{42,47,40, 48}. Studies are showing that peloids are effective in such diseases^{22, 23, 24}. The connection between the positive effect of peloids in other dermatological pathologies with the

microbiota in it has not been evaluated much⁷. The microbiota contained by peloids is quite likely to be effective on pathogenic species. Therefore, it is thought that the phyto-pelodies that will occur when mixed with medicinal plants will have a higher antimicrobial effect. On the other hand, it is also possible that the antimicrobial effect of plants will affect the peloid flora and disrupt its natural structure. There is a related data deficiency in the literature. Accordingly, it is thought that the production of phyto-peloids and their effects are extremely important. But these studies mostly remain at the preclinical level. While in order to have sufficient evidence, it should be supported by clinical research.

CONCLUSION

It is a fact that when an evaluation is made in the light of scientific data, official explanations and practices and market researches, mud has been used in the health and cosmetics industry for many years with pure, processed or additives.

When we look at around 1300 thermo-mineral water sources, hundreds of small lakes and deltas and thousands of years of Anatolian geography that we know exist in our country, we see that the number of muds licensed by the Ministry of Health is still around 10 and there is no inventory of our country. In the scientific community, the number of articles related to mud does not exceed several.

In an environment where the world's demand for natural treatments and natural care products has increased so much, we must recognize our presence in mud and combine mud with natural medicinal plants to create innovations in the field of health and cosmetics. Also, turning this into an investment and earning will undoubtedly be possible by doing more researches in this field. Integrating mud into spa tourism and making mud

an indispensable product of every region and every facility requires creating unique products and treatment-care packages with medicinal plants, recognizing mud and medicinal plants and using them correctly. In this regard, determining the potential of our country and activating this potential is necessary for the future.

As mentioned above, it is known that there is a synergistic effect in the treatment mechanisms of herbal products. The compounds they contain are involved in the treatment process in coordination. Accordingly, it can be said that the use of mud with medicinal plants will be more effective than its use alone. Mud treatment should be combined with different medicinal plants on related diseases and the results should be compared with its use unaccompanied.

Mud is a well-expanded health and cosmetic product with its known varieties and materials such as various herbs, essences, oils, fruit extracts etc. added to it. Empirical use of mud, which is a miracle of nature, for thousands of years, has been proven as a result of scientific studies on its contribution to human health and care. Determining the mud sources existing in our country, taking inventory, determining the necessary tests, medical and cosmetic benefits will undoubtedly be possible with the further study and production of our scientists. We hope that this study will increase awareness of the subject and will enable scientists to conduct more scientific research and produce scientific publications on mud sources and natural plants in their region. The fact that our official institutions and organizations also focus on mud and natural plants while carrying out their duties, to produce joint projects with scientific communities and to support scientific projects, will result in the use of these important values of our country more rationally for the benefit of humanity.

REFERENCES

1. Oyuryüz ZŞ, Gürel A. Humik maddelerin sağlık sektöründe kullanımı ve girişimcilik faaliyetleri. *SAU Fen Edebiyat Dergisi*. 2012; 1.
2. Dönmez A. Balneoterapi yöntemleri. *Balneoloji ve Kaplıca Tıbbı. İstanbul: Nobel Tıp Kitabevleri*. 2002: 57-64.
3. Gürdal H. Peloidler. *Balneoloji ve Kaplıca Tıbbı. İstanbul: Nobel Tıp Kitabevleri*. 2002: 97-112

4. <https://www.satirk.gov.tr.turkiye>.
5. Çelik-Karakaya M, Karakaya N. Kaplıca Tedavisinde Kullanılan Termal Çamurların Uygunluğunu Belirleyen Parametreler. *1. Tıbbi Jeoloji Çalıştayı Kitabı*. 2009: 31-43.
6. Quintela A, Terroso D, da Silva, E.F, et al. Certification and quality criteria of peloids used for therapeutic purposes. *Clay Minerals*. 2012; 47(4):441-451
7. Pesciaroli C, Viseras C, Aguzzi C, et al. Study of bacterial community structure and diversity during the maturation process of a therapeutic peloid. *Applied Clay Science*. 2016; 132: 59-67.
8. <https://hsgm.saglik.gov.tr/tr/cevresagligi-suguvenligi/su-guvenligi-ve-kaplicalar-birimi/peloid-nedir.html>
17.02.2020
9. Gürdal H. Peloid uygulamaları. *Balneoloji ve Kaplıca Tıbbi. İstanbul: Nobel Tıp Kitabevleri*. 2002: 107-110.
10. Karagülle MZ. Kaplıca tedavisi, balneoterapi ve hidroterapi. *Kaplıca Tıbbi ve Türkiye Kaplıca Rehberi. İstanbul: Nobel Tıp Kitabevleri*. 2011: 1-21
11. Martínez-Villegas N, Muñoz MS, González-Hernández P, et al. Inorganic and organic characterization of Santa Lucía salt mine peloid for quality evaluations. *Environmental Science and Pollution Research*. 2019: 1-15.
12. <http://konyaeah.saglik.gov.tr/TR.278802/tibbi-camur-tedavisi.html>.
13. Barassi G, Obrero-Gaitan E. Integrated Thermal Rehabilitation: A New Therapeutic Approach for Disabilities. *Adv Exp Med Biol*. 2020; 1251: 29-38
14. Angioni MM, Denotti A, Pinna S. Spa therapy induces clinical improvement and protein changes in patients with chronic back pain. *Reumatismo*. 2019 Oct 24; 71(3):119-131.
15. Varzaityte L, Kubilius R, Rapoliene L. The effect of balneotherapy and peloid therapy on changes in the functional state of patients with knee joint osteoarthritis: a randomized, controlled, single- blind pilot study. *Int J Biometeorol*. 2019 Sep 6. doi: 10.1007/s00484-019-01785-z
16. Min KJ, Choi H, Tae BS, et al. Short-term benefits of balneotherapy for patients with chronic pelvic pain: a pilot study in Korea. *J Obstet Gynaecol*. 2019 Aug 28; 1-6. doi: 10.1080/01443615.2019.1631771.
17. Király M, Kóvári E, Hodosi K, et al. The effects of Tiszasüly and Kolop mud pack therapy on knee osteoarthritis: a double-blind, randomized, non-inferiority controlled study. *Int J Biometeorol*. 2019 Aug 3. doi: 10.1007/s00484-019-01764-4
18. Cozzi F, Galozzi P, Ciprian L. Mud-bath treatment of seronegative spondyloarthritis: experience at the Eugeanean Thermal Area. *Int J Biometeorol*. 2019 Jul 24. doi: 10.1007/s00484-019-01761-7.
19. Toppide LJ, Perper M, Keri JE. Treatment of seborrheic dermatitis: a comprehensive review. *J Dermatolog Treat*. 2019 Mar; 30(2):158-169. doi:10.1080/09546634.2018.1473554.
20. Hamed S, Almalty AM. Skin tolerance of three types of dead sea mud on healthy skin: a short-term study. *J Cosmet Sci*. 2018 Jul / Aug; 69 (4): 269-278.
21. Cozzi F, Raffener B, Beltrame V. Effects of mud-bath therapy in psoriatic arthritis patients treated with TNF inhibitors. Clinical evaluation and assessment of synovial inflammation by contrast-enhanced ultrasound (CEUS). *Point Bone Spine*. 2015 Mar; 82 (2): 104-8. doi: 10.1016/j.jbspin.2014.11.002.
22. Riyaz N, Arakkal FR. Spa therapy in dermatology. *Indian J Dermatol Venereol Leprol*. 2011 Mar-Apr; 77 (2): 128-34. doi: 10.4103/0378-6323.77450.
23. Costantino M, Lampa E. Psoriasis and mud bath therapy: clinical-experimental study . *Clin Ter*. 2005 Jul-Aug; 156 (4): 145-9.
24. Carabelli A, De Bernardi di Valserra G, De Bernardi di Valserra M. Effect of thermal mud baths on normal, dry and seborrheic skin. *Clin Ter*. 1998 Jul Aug; 149 (4): 271-5.
25. Therkleson T. Topical ginger treatment with a compress or patch for osteoarthritis symptoms. *J Holist Nurs*. 2014;32(3):173–182. doi:10.1177/0898010113512182.
26. Lapane KL, Sands M, Yang S, et al. Use of complementary and alternative medicine among patients with radiographic confirmed knee osteoarthritis. *Osteoarthritis Cartilage*. 2012 Jan;20(1):22-8. doi: 10.1016/j.joca.2011.10.005.
27. Dragos D, Gilca M, Gaman L, et al. Phytomedicine in joint disorders. *Nutrients*. 2017 Jan 16;9(1). pii: E70. doi: 10.3390/nu9010070.
28. Shenefelt PD. Herbal treatment for dermatologic disorders. *Herbal Medicine: Biomolecular and Clinical Aspects*. 2nd edition.
29. Hussain Z, Thu HE, Shuid AN, et al. Phytotherapeutic potential of natural herbal medicines for the treatment of mild-to-severe atopic dermatitis: A review of human clinical studies. *Biomed Pharmacother*. 2017 Sep;93:596-608. doi: 10.1016/j.biopha.2017.06.087.
30. Amparo TR, Seibert JB, De Abreu Vieira PM, et al. Herbal medicines to the treatment of skin and soft tissue infections: advantages of the multi-targets action. *Phytotherapy Research*. 2019;1–10. doi: 10.1002/ptr.6519
31. <https://ticaret.gov.tr/data/5b87000813b8761450e18d7b/Kozmetik.pdf> 17.02.2020



32. http://megep.meb.gov.tr/mte_program_modul/moduller_pdf/Basic%20Kozmetik.pdf 17.02.2020
33. Bone K, Mills S. Principles and practice of phytotherapy: modern herbal medicine. 2nd edn. Churchill livingstone: Edin-burgh (UK).
34. Stepień AE, Gorzelany J, Matłok N. et al. The effect of drying methods on the energy consumption, bioactive potential and colour of dried leaves of Pink Rock Rose (*Cistus creticus*). *J Food Sci Technol*. 2019;56:2386–2394. <https://doi.org/10.1007/s13197-019-03656-2>
35. Choi, S. Epidermis proliferative effect of thePanax ginseng Ginsenoside Rb 2. *Archives of pharmacal research*, 2002;25(1):71-76.
36. Kim W K, Song SY Oh WK, et al. Wound-healing effect of ginsenoside Rd from leaves of Panax ginseng via cyclic AMP-dependent protein kinase pathway. *European journal of pharmacology*, 2013;702(1-3):285-293.
37. Das T, Debnath J, Nath B, et al. Formulation and evaluation of an herbal cream for wound healing activity. *Int J Pharm Pharm Sci*, 2014;6:693-7.
38. Finberg MJ, Muntingh GL, Van Rensburg CE. A comparison of the leaf gel extracts of Aloe ferox and Aloe vera in the topical treatment of atopic dermatitis in Balb/c mice. *Inflammopharmacology*. 2015;23:337–341.
39. Sirikudta W, Kulthanan K, Varothai S, et al. Moisturizers for patients with atopic dermatitis: an overview. *J Allergy Ther*. 2013;4(4), 1-6.
40. Chew YL, Al-Nema M, Ong VWM. Management and treatment of atopic dermatitis with modern therapies, complementary and alternative medicines: A review. *Oriental Pharmacy and Experimental Medicine*, 2018;18(2):67-76.
41. Theoharides TC, Stewart JM, Tsilioni I. Tolerability and benefit of a tetramethoxyluteolin-containing skin lotion. *International journal of immunopathology and pharmacology*, 2017;30(2):146-151.
42. Bomstein Y, Rozenblat S. Treatment of atopic dermatitis with KAM-3008, a barrier-based, non-steroidal topical cream. *Journal of Dermatological Treatment*. 2015;26(5):426-430. doi: 10.3109/09546634.2015.1021238
43. Altındış M, Aslan FG, Uzuner H, et al. Zeytin yaprağı ekstresi ve propolisin herpes simpleks virüsü tip 1 üzerine antiviral etkisinin asiklovir ile karşılaştırılması. *Mikrobiyol Bul*. 2020;54(1):79-94.
44. Jautová J, Zelenková H, Drotarová K, et al. Lip creams with propolis special extract GH 2002 0.5% versus aciclovir 5.0% for herpes labialis (vesicular stage). *Wiener Medizinische Wochenschrift*. 2019;169(7-8):193-201.
45. Kalaaji AN, Wahner-Roedler DL, Sood A, et al. Use of complementary and alternative medicine by patients seen at the dermatology department of a tertiary care center. *Complementary therapies in clinical practice*. 2012;18(1):49-53.
46. Murphy EC, Nussbaum D, Prussick R, et al. Reply to:“Response to:‘Use of complementary and alternative medicine by patients with psoriasis’”. *Journal of the American Academy of Dermatology*. 2019;81(4) e107-e110.
47. Wu J, Li H, Li M. Effects of baicalin cream in two mouse models: 2, 4-dinitrofluorobenzene-induced contact hypersensitivity and mouse tail test for psoriasis. *International journal of clinical and experimental medicine*. 2015;8(2):2128-37
48. Chiang CC, ChengWJ, Lin CY, et al. Kan-Lu-Hsiao-Tu-Tan, a traditional Chinese medicine formula, inhibits human neutrophil activation and ameliorates imiquimod-induced psoriasis-like skin inflammation. *Journal of ethnopharmacology*. 2020;246:1122-46.