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Dermatology Benefits of Punica Granatum: A Review of the Potential Benefits of Punica Granatum in Antiacne Activity

[1] Sourav Khawas, [2] Manmohan Sharma, [3] Rajiv kukkar, [4] Anil Sharma

[1] PG Department of Pharmaceutics,

[2] Associate Professor, Department of Pharmaceutics,

[3] Principal, Department of Pharmacognosy,

[4] Associate Professor, Department of Quality Assurance

School of Pharmaceutical Studies Faculty of Health Sciences, Dr. K.N Modi University, Newai (Tonk) Rajasthan

ABSTRACT

Acne vulgaris is the skin condition that affects people the most often in a generation. Acne vulgaris is a common chronic skin condition that affects the hair follicles and sebaceous gland that they are attached to. Teenagers and young adults are the age groups when acne most frequently occurs and manifests as red, painful bumps with pus-filled pimples. Some medicinal plants are readily available and safer than others, making them suitable anti-acne treatments. Herbs with varied antibacterial, anti-inflammatory, antifungal, and antioxidant properties have been used to treat acne. Overall, compared to modern pharmaceuticals, herbal therapy is still far more affordable and safe. Therefore, in the current environment, there will be a greater need for herbal therapeutic products than for synthetic ones.

INTRODUCTION

Herbal cosmetics

There will be desperate changes in the society are clearly seen in all parts of the world for enormous application of cosmetics for the most part in 21st century. The world cosmetics is derived from Greek word “KOSMETICOS” which define adorn and preparation. Cosmetics are external preparation meant for to apply on external part of body that is nails, skin, and hair for colouring, covering, softing, cleaning, nourishing, waving setting, mollification, preservation, removal and protection. Cosmetics can be applied by rubbing, pouring, sprinkling or spraying on human body or any part for cleansing, beautifying, promoting attractiveness altering appearance [1, 2]

Cosmetics are the chemical compounds derived from either natural sources or synthetically created products. Cosmetics are those designed for personal care and skin care which is used to protect the body skin. These are also designed to enhance the persons appearance and also used to conceal blemishes by enhancing the persons natural features such as eyebrows, eyelashes. Cosmetics are also mainly designed to enhance the fragrance of the

body. Medicinal plants by virtue of their safe nature and easy availability may lend themselves as potential anti-acne therapy. The present review deals with the proven medicinal plants to treat acne.

Acne

Inflammation of the pilo sebaceous unit causes acne, which has a chronic history and is self-limiting. Under the influence of normally circulating dehydroepiandrosterone (DHEA), Cutibacterium acne causes acne vulgaris in adolescents. This common skin condition primarily affects the face, although it can also affect the upper arms, trunk, and back. It can cause both inflammatory and non-inflammatory contusions [3].

Long-term skin condition acne, commonly known as acne vulgaris, is caused by clogged hair follicles by oil production and dead skin cells. Blackheads, whiteheads, nodules, and other types of papules are caused by hair, sebum bacteria, and dead skin cells blocking the pores in the skin. Acne is a chronic skin condition. At some point, most teenagers will get papules. Some have a limited number of papules that go away quickly. Others get persistent acne that is clearly noticeable. Particularly throughout puberty, this can be extremely distressing.

It is the most common skin disease worldwide, being specifically common in adolescents and young adults. However, it can also affect toddlers and adults at any age. This assess the pathophysiology, topical and oral treatments, therapeutic approaches and evolving therapeutics for acne. Acne vulgaris, a disease of pilosebaceous follicles is an extremely common clinical problem. In societies, acne vulgaris is a nearly universal skin disease, affecting 79% to 95% of the adolescent population. Though it is more prevalent among men than women at age 18, beyond the age of 23 clinical acne is more prevalent among women as the prevalence in men gradually declines. At 40 to 49 years, 3% of men and 5% of women still have definite, mild, clinical acne, and at 50 to 59 years, 6% of men and 8% of women have physiologic acne [4, 5].

Four major factors are involved in the pathogenesis:

- Increased sebum production
- Hyper cornification of the pilosebaceous duct
- Abnormality of the microbial flora, especially colonization of the duct with Propionibacteriumacnes
- Inflammation

It has been demonstrated that acne sufferers' sebum is lacking in the vital fatty acid linoleic acid. The retention hyperkeratosis of the pilosebaceous follicle is linked to this deficit. After the follicles get clogged, bacteria—particularly the Gram-positive anaerobic diphtheroid P. acnes—produce lipases, which break down sebaceous gland triglycerides into free fatty acids. These bacteria occupy the follicles during adolescence but do not attack living tissue. These acids subsequently cause a neutrophilic inflammatory response when they are extruded into the dermis through the dilated follicular wall along with bacterial proteins and minute pieces of keratin [6].

ADVANTAGES OF ANTIACNE

- Antibacterial, anti-inflammatory, anti-oxidant activity.
- Decreasing the excess sebum production
- Correcting altered follicular keratinisation.
- Clears clogged pores of impurities, oil and dust.
- Treats active acne and prevents further breakouts

List of some medicinal plants related to anti-acne activity.

Common name	Biological sources	Parts to be used	Uses
Aloe Vera	Aloe barbadensis	Leaves	Skin abrasions, Minor burns
Honey	Apis Mellifera	Juice	Anti-oxidant, Anti inflammatory
Pomegranate	Punica granatum L.	Seeds, flowers	Antiacne, Anticancer
Black Cumin	Nigella sativa	seeds	Antihypertensive, Antibacterial
Bitter Almond	Prunus amygdalus Batsch var. amara	seeds	To treat cough, spasms
Tea Tree	Melaleuca Alternifolia	Leaves	Treatment of nail fungus, insect bites and acne
Blue Gum	Eucalyptus globulus	Leaves	Antiseptic, Antioxidant
Rosemary	Rosmarinus officinalis	Leaves, Twigs	Anti-bacterial, Antioxidant

Neem

Neem is an essential medicinal plant which belongs to Meliaceace family originated from Azadiracta indica. Neem is mainly constituted of Azadirachtin, nimbin, azadirone, methyl stearate, salannin, meliantriol. The major parts which are medicinally used in neem plant are flowers, leaves, seeds, bark. Neem has various medicinal activity such as Anthelminthic, Anticancer, neem has the ability to heal ulcers in the digestive tract, it also acts as antibacterial. The leaf extract is used to reduce tooth plaque and to treat lice, neem also contains chemicals that might help to reduce blood sugar levels [7, 8].

Ashwagandha

Ayurveda, the traditional Indian medical system, considers ashwagandha to be its most significant herb. Indian ginseng or winter cherry are the names most people use to refer to it. It mainly derived from the Solanaceae family plant Withania somnifera. Alkaloids like isopelletierine, anaferine, and anahygrine are among the several chemical components of ashwagandha that are clearly present. Steroid lactones like withanoloides and withaferine were also constituents of it. Apart from acyl steryl glucosides, saponins, and sitoindosides, withania somnifera also contains these main components. The ashwagandha plant contains medicinally active elements in its fruits and berries. Its roots also have unique medicinal properties that are employed in a variety of herbal medicines. In the context of herbal cosmetics and medications nowadays, it has a wide range of applications. The benefits of ashwagandha for treating several inflammatory illnesses are mostly evident. It is therefore typically employed as a plant ant inflammatory agent. As mentioned in the previous section, ashwagandha and its extract have a strong antioxidant effect that is very useful when making different types of cosmetics, such anti-acne cream [9].

Hemp

Despite having a psychotropic effect on humans, the hemp plant is a robust, aromatic, tall annual herb that is a member of the cannabaceae family. Additionally, it contains some cosmeceutical properties that are used in many cosmetic preparations. Cannabis sativa is the plant from which hemp is often derived. Every portion of the hemp

plant has a unique medicinal quality. Certain have medical properties, while others are cosmeceutical. The majority of seed powders have unique properties that help with acne, pimples, and other skin conditions. Hemp has cellulose (53–91%), hemicellulose (4-6%), pectin (1-3%), and lignin as its main chemical elements. Additionally, it contains the majority of acids, including cannabic chromic acid, cannabinolic acid, and cannabinodiolic acid.

Camphor

According to recent studies and research, the traditional medical system plays a significant role in treating the human health care system, which has become favourable because the pharmaceuticals used in it are more readily available and have less harmful side effects. Terpenes like camphor are often obtained from the Cinnamomum camphor tree, which is a member of the Lauraceae family. The wood of the huge, east Asian evergreen camphor laurel tree contains camphor. Camphor will have a huge variety of chemical compounds, each of which has a different medical application. Linalon, lineole, beta pinene, and alpha terpineol make up the majority of the chemical composition. Although camphor has several uses in the human medical system, its primary usage is in the treatment of some very serious skin disorders. It is possible to reduce skin irritation and itching by using lotions and creams that contain camphor as their main ingredient. Additionally, because of its antibacterial and antifungal qualities, it can be used to treat a variety of UV light-induced skin disorders, including wrinkles and acne. It can also improve the overall appearance of skin. Because camphor has a strong anti-aging effect, it is frequently used in various cosmetic formulas, including lotions and creams for acne [10].

Pomegranate

Pomegranate has numerous medicinal activities, such as anti-diabetic, anti-inflammatory, anti-malarial, anti-fungal, and anti-bacterial. It also has effects such as improving the gastrointestinal tract microbiota, preventing obesity, and improving fertility in men. Pomegranate is further used to treat some diseases, such as cardiovascular problems, cancer, depression, and wound healing.

Fruit peel powder is used to accelerate wound healing, as a purgative, and to relieve indigestion. Astringents, laxatives, and blood purifiers are all found in pomegranate fruit. In traditional medicine, leaves, fruits, fruit skin, and seeds are commonly used for various diseases.

Figure 1. Pomegranate tree, flower, and fruit

Phytochemistry

Pomegranate pericarp has a high amount of phytochemicals, mainly polyphenolic flavonoids, and ellagitannins, containing ellagic acid and punicalagin. Pomegranate contains phytochemical compounds in its diverse parts, which have several pharmacological functions.

Pomegranate juice

Anthocyanin creates an attractive purple-red color in pomegranate juice, which is reduced during the pressing process. The amounts of fatty acids, sterols, organic acids, triterpenoids, and minerals content have been also reported in pomegranate juice. In general, pomegranate has two main composition groups: [11, 12].

Polyphenols

Hydrolysable tannins are the principal group of pomegranate polyphenols, which consist of gallotannins, ellagitannins, galagyl esters, hydroxycinnamic acids, and hydroxybenzoic acids.

The prime ingredient of ellagitannins is punicalagin, which is mostly recognized in the pericarp, peel, flowers and seeds. In addition, punicalagin and its isomers, pomegranate contains punicalin A, punicalin B, and pedunculagin isomers. Likewise, Gallic acid, ellagic acid, caffeic acid, chlorogenic acid, p-coumaric acid, aglycone, and ferulic acid are present in pomegranate.

Granatum in traditional medicine

In traditional medicine, pomegranate peel, flowers, branches, and roots are used. All P. granatum L. components have strong astringent effects due to the presence of abundant tannins. Several pomegranate flower infusions and decoctions of the flowers have been utilized to remedy diarrhea and vaginal infectious discharge. In addition, the extract of pomegranate peel has been used to treat acute pancreatitis.

Fresh pomegranate juice is use for remedy of gall bladder problems and its decoction is useful for any types of diarrheas, either simple or bloody diarrhea and stomach discomfort. Alkaloid substances in pomegranate root bark and ethanolic extract are used to eliminate intestinal parasites. Also, its antibacterial and anti-inflammatory effects was utilized in traditional medicine

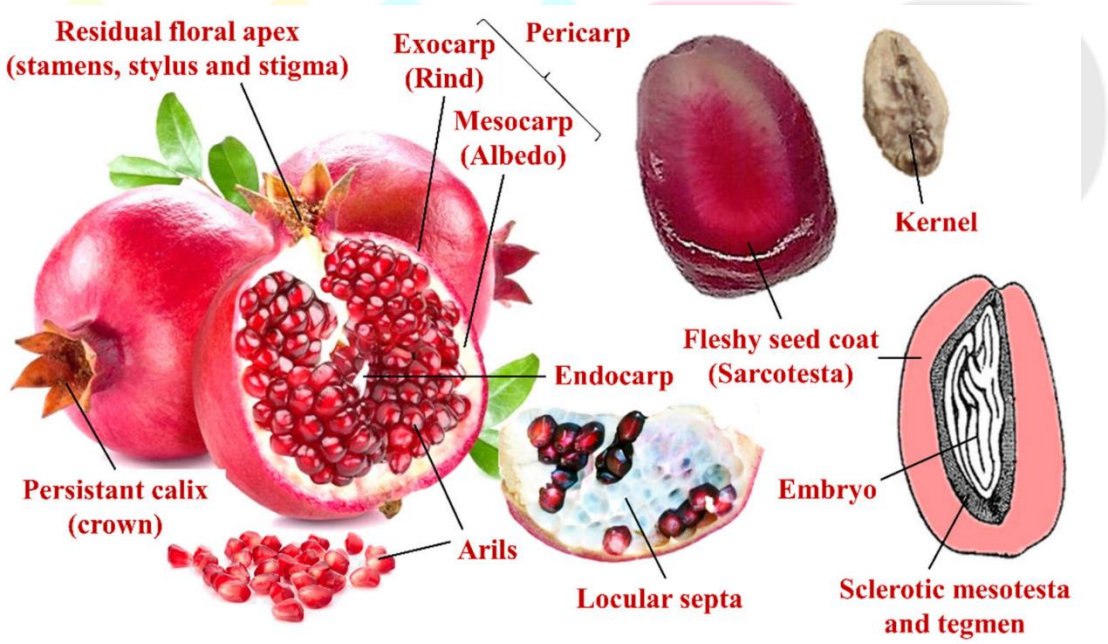

Fig. 2. The commonly main Anthocyanosides ingredients in P.granatum

Anthocyanosides

They are the next important component group found in the fruit and blossom and are responsible for the crimson hue of the arils. Anthocyanin, which is abundant in pomegranates, has a strong antioxidant potential. The main function of anthocyanins is as key antioxidants.

Pomegranate seed oil (PSO)

30.12% punicic acid, 28.92% linoleic acid, 19.01% oleic acid, 1.49% gadoleic acid, 0.18% erucic acid, 0.18% linolenic acid, and 0.07% palmitoleic acid are all present in PSO [7, 8].

Pomegranate peels

Tannins are water-soluble and hydrolysable phenolic compounds found in pomegranate skin in a variety of forms. Four primary groups of tannins are identified by the structure: gallotannins, ellagitannins, complex tannins, and thick tannins. Punicalagin, a ellagitannin with a far higher quantity than other compounds, is the main constituent of pomegranate peels.

P. granatum in traditional medicine

In traditional medicine, pomegranate peel, flowers, branches, and roots are used. All P. granatum L. components have strong astringent effects due to the presence of abundant tannins. Several pomegranate flower infusions and decoctions of the flowers have been utilized to remedy diarrhea and vaginal infectious discharge. In addition, the extract of pomegranate peel has been used to treat acute pancreatitis. Fresh pomegranate juice is use for remedy of gall bladder problems and its decoction is useful for any types of diarrheas, either simple or bloody diarrhea and stomach discomfort. Alkaloid substances in pomegranate root bark and ethanolic extract are used to eliminate intestinal parasites. Also, its antibacterial and anti-inflammatory effects was utilized in traditional medicine [10].

P. granatum in dermatology

P. granatum L. is a shrub that contains specific components in particular polyphenols and anthocyanins, which have antioxidant, anti inflammation, wound healing, whitening, antiacne, anti-hair loss, antiviral, and antibacterial effects. It also prevents skin photoaging due to UVB.

Wound healing activity

Several research have proven P. granatum improve wound repairing process. Nayak et al. assessed the wound repairing process of P. granatum fruit peel. In this study, a 95% decreasing wound area was reported on animals treated by the extract compared with 84% at control group. Skin epithelialization in pomegranate extract-treated group was faster than control group, and the content of hydroxyproline in pomegranate extract-treated group was remarkably greater than the control group. As a result, P. granatum significantly improved wound healing in rats.

In addition, Murthy KN et al. discovered that pomegranate extract had high phenolic compounds (44%). They formulated a 10% water-soluble gel to investigate wound healing, skin contraction percentage, collagen, and hydroxyproline content in a rat skin model. Rats treated with 2.5% gel showed a mean improvement of 55.8% and 40.8% compared to the positive and negative control groups, respectively. Whilst, with 5.0% gel group exhibited well repairing of 59.5% and 44.5% in comparison to the negative and positive controls, respectively. Hydroxyproline content was enhanced in the 5% gel treatment. Histological evaluation confirmed wound repairing in the use of gels containing extracts. The content of hydroxyproline in the 5% gel increased twice as well as histopathological evaluation support wound healing with the use of gels. The wound healing was by 5.0% gel, 5.2% gel, and control, 10, 12, and 16 to 18 days, respectively. Chromatography results showed catechin and gallic acid as the main components of their repair.

In a study, ointments of methanolic extract of P. granatum at 10%, and 15% w/w were investigated for the effect of wound healing in a cut wound model of rats. The results were as same as those of nitrofurazone ointment. Wound contraction activities of 10% and 15% P. granatum ointments were 97.8%, and 98.4%, respectively, and significantly ($P < 0.05$) higher than the control. In the 15% w/w pomegranate extract ointment group, wound closure time and wound contraction percentage were lower and higher, respectively. In the 10% pomegranate extract ointment group, wound contraction was significantly observed on the 18th day and wound closure time attained 100% on the 20th day. Therefore, methanolic extract of pomegranate demonstrated as a potential wound healing agent.

Anti-inflammatory activity

Ellagic acid (EA) possess anti-inflammation effects in chronic disorders. Also, Ellagic acid treatment suppresses inflammation responses on keratinocytes by regulation vital inflammation signaling pathways like mitogen-activated protein kinases, signal transducers, and activators of transcription (STAT). In vivo tests on a DfE-induced Atopic dermatitis mice exhibited that the EA improved skin signs by reducing inflammatory responses. Therefore, EA can be a potential alternative treatment for atopic dermatitis by inhibiting inflammatory signaling pathways. Due to several risks related to NSAIDs for the remedy of pain and inflammation, medicinal plants are used as alternative therapies. Ben Saad et al. showed that ellagic acid, gallic acid, and punicalagin A&B potentially inhibited the production of NO PGE-2, and IL-6 induced by LPS, and probably ellagic acid, gallic acid, and punicalagin which are the most important components of pomegranate and they are probably responsible for role anti-inflammatory[10, 12].

Antibacterial and antimicrobial activity

Tannins may show their antimicrobial activity via three mechanisms: inhibition enzymes function, precipitation of membrane proteins, and reduction of metal ions

Herpes disease is always in need of new and effective treatment products, Therefore, Houston et al. evaluated the activity of pomegranate fruit and zinc metal ions on herpes simplex. In this study, the effect of this compound on herpes simplex type 1 and acyclovir-resistant herpes in host cells of Vero was done by MTS method and commercial kit. Zinc sulfate, zinc citrate, zinc stearate, and zinc gluconate indicated increased antiviral activity similar to PRE against HSV-1 up to 4 times. Punicalagin had eight times more antiviral activity than an equivalent mass of pomegranate rind extract (PRE). Even so, the antiviral information displayed that punicalagin has viricidal activity remarkably lower than that of PRE, which is comparable to acyclovir.

Likewise, PRE exhibited its potential versus acyclovir-resistant HSV, whilst acyclovir exhibited no potency. The enhanced antiviral action of PRE in combination with Zn (II) has the potential as an innovative topical drug versus HSV infections like cold sores P. granatum has known as an herbal drug with potential antimicrobial activity. Recently, Houston DM et al. has been indicated that the antiviral effect of pomegranate rind extract is striking increased with zinc (II) ions with a potency of up to 7 log decline versus herpes simplex virus (HSV) [13].

Skin whitening activity

P. granatum extract-containing topical microemulsion regulates people's skin melanin levels as well as erythema and redness. P. granatum exhibits considerable effectiveness in suppressing free radicals, which is consistent with its substantial content of polyphenolic chemicals. It is thought that ellagic acid chelates copper in tyrosinase, which brightens the skin. This study demonstrates that a topical formulation for skin patches and erythema could make use of the P. granatum extract microemulsion.

Today, there are many effective ingredients and skin-lightening products that may inhibit tyrosinase activity in the melanogenesis process. Tyrosinase inhibitors in particular hydroquinone, kojic acid, and arbutin may induce skin irritation or acute dermatitis, and there are many concerns about the safety of these agents.

Thus, the need for safe and effective natural skin lightening agents has increased more than ever. Pomegranate fruit extract contains substances that inhibit melanogenesis and shows its potential to be used as a lightening cream in cosmetic formulations. punicalagin is a polyphenolic compound in pomegranate fruit extract, that has been recognized as a melanin production inhibitor.

Anti-acne activity

Skin conditions like acne vulgaris are common and are characterised by high sebum production, hyperkeratosis, Cutibacterium acnes, Staphylococcus aureus, and inflammation. Pomegranate extract significantly reduced edoema caused by C. acnes in the Wistar rats' ears, according to research by Lee et al.

Their results represented that pomegranate extract inhibited bacterial growth and lipase function. Four hydrolysable tannins are punicalagin, punicalin, strytinin A, and also granatin B. Punicalagin and punicalin compounds had antibacterial properties and testosterone-induced HaCaT proliferative effects more than others. punicalagin, strictinin, and granatin B showed lipase inhibitory effects. Granatin B compound causes downregulation of cyclooxygenase-2 expression and prostaglandin E2 production in RAW 246.7 cells treated with P. acnes [14, 15].

Conclusion

The pomegranate Punica granatum L. has unique chemicals called polyphenols and anthocyanins that have the ability to be antibacterial, antioxidant, wound healing, whitening, and healing from acne. It also guards against the infection of the herpes simplex virus and stops UVB-induced skin photoaging.

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