

MIMOSA PUDICA: UNVEILING ITS POTENTIAL IN COSMETICS

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ABSTRACT

Mimosa pudica Linn. is commonly known as the “Sensitive Plant” and “Touch me not”. It is a domestic plant, under-explored, in the cosmeceutical industry, and found to be fewer side effects. Recently it has attracted attention for its use in the cosmetic industry with a special focus on anti-aging and skincare formulations. This article explores the extensive phytochemical profile of the plant involving alkaloids, flavonoids, tannins, and phenolic compounds which contribute to its antioxidant, antimicrobial, anti-inflammatory, and UV protective activities. For instance, being able to elevate collagen synthesis, enhance skin elasticity, and provide detoxification effects are among the important attributes that make *Mimosa pudica* an invaluable natural ingredient in cosmeceuticals. Geographically, this plant has a wide distribution across the globe; due to its ease of cultivation, adapts well to various climatic condition thus ideal for sustainable beauty products. Consequently, *Mimosa pudica* is expected to play an increasing role within contemporary skincare formulas as customers turn towards more organic, economic, and eco-friendly cosmetics.

Keywords:

INTRODUCTION

The regulation of the European Commission, 2015, defines cosmetics as 'any substance or mixture intended to be placed in contact either directly or indirectly with external parts of the human body, such as epidermis, hair, nails, lips, and external genital organs, or with teeth and mucous membranes of the oral cavity, with a view exclusively or mainly to cleaning the skin; to perfuming the body, to change the appearance; to protect or to modify the skin's structure; to keep it in good condition; or to correct body odors'. Cosmetics hold an important position in modern society.[1] Cosmeceuticals is a term referring to skincare products that have been engineered to contain active ingredients, such as alpha-hydroxy acids, retinoic acid, ascorbic acid, and coenzyme Q10. [2] These active ingredients help in different ways to make your skin more elastic, delay age-related wrinkles and changes of the skin, provide antioxidant protection by neutralizing free radicals, which are produced by UV radiation, and control the degradation of collagen.[3] The 20th century was the time of synthetic and chemically modified products swarming the cosmetics marketplace. However, at the close of the last century and the beginning of this new century, consumers began to demand organic or natural ingredients in cosmetic formulations. In the last couple of years, there's been an increasing march toward more sustainable products, really focusing on consumer benefits with reduced or minimized environmental impact.[4]The cosmetic industry has recently turned to nature as a source of safer and more effective products. There has been a noticeable transition to plant-based formulations, likely due to rising consumer awareness of the negative effects of synthetic chemicals utilized in traditional cosmetic products. Contemporary cosmeceuticals are using the tried-and-true medicinal herbs that have been utilized for thousands

of years in traditional medicine. Plant extracts containing bioactive compounds can protect the skin from environmental damage and promote skin renewal, potentially reversing acne and premature aging. As a result, new eco-friendly beauty products are being developed at a rapid pace by the cosmetics industry around the world.[5] Worldwide, between 60-80 percent of the population in underdeveloped nations relies on medicinal plants for their primary healthcare, according to the World Health Organization (WHO).[6] This dependency highlights the fact that plants offer medicinal properties that are currently being explored in the cosmetic industry. Thanks to advancements in extraction technology, phyto-constituents may now be extracted from plants and used in a wide variety of cosmetic goods.[5] Using these plant-based compounds in anti-aging serums or skin-soothing creams can satisfy consumers' desires for a natural, effective product. *Mimosa pudica* Linn, dubbed the "Sensitive Plant" because its sensitivity to touch, is one of the plants that is attracting a lot of interest. The name "Mimosa" is derived from the Greek word for "mimic", while "pudica" comes from the Latin for "shy." This plant has quite an interesting behavior, in that when its leaves are touched or otherwise disturbed, they actually fold up as if shy or mimicking a response. [7] In Hindi, it is called "Lajwanti" or "Chuimui" in local dialects. *Mimosa pudica* has a long history of usage in Ayurveda and traditional medicine for the treatment of skin conditions, wounds, and infections; and is presently being studied for its cosmetic properties due to its abundance of bioactive chemicals.[8]

The leaves of this plant are bipinnately complex, comprised of 10-20 pairs of tiny, digitated leaflets. Vegetative peduncles are rough and produce flat, bristly pods with 3–5 seeds. The plant thrives on well-drained, sun-exposed soils at tropical and subtropical geographical areas. [8] Investigation of the phytochemical composition of *Mimosa pudica* revealed elevated concentrations of alkaloids, C-glycosides, flavonoids, tannins, sterols, terpenoids, and fatty acids. Non-protein amino acids such as mimosine enhance its therapeutic properties. Therefore mentioned chemicals possess antioxidant, anti-inflammatory, antibacterial, and wound-healing characteristics. Bioactivities such as these are essential for cosmetics since they safeguard, revitalize, and improve the appearance of the skin. [9] Throughout millennia, the roots and leaves of *Mimosa pudica* have been employed for the treatment of gastrointestinal and neurological disorders. The plant has been topically used for the treatment of snake and scorpion stings, leukoderma, smallpox, inflammation, and wounds. The objective of modern cosmeceuticals is to reinstate the integrity of the skin and accelerate the healing process. [10]

Scientific

Classification:

Kingdom: Plantae

Division:

Magnoliophyta **Class:**

Magnoliopsida **Order:**

Fabales

Family : Fabaceae Subfamily:Mimosoideae

Genus : **Mimosa**

Species: *M.pudica*

Recent investigations by researchers have substantiated the aesthetic advantages of the plant. The antioxidant properties of *Mimosa pudica* counteract the harmful effects of free radicals that contribute to skin aging. Given its anti-inflammatory properties, it is well-suited for skin types that are sensitive or inflamed. The natural antibacterial properties of the plant can be utilized in the treatment of acne and other skin conditions. The capacity to enhance collagen synthesis and skin suppleness renders it a highly beneficial component for anti-aging skincare. Topical pharmaceutical formulations such as lotions, gels, and emulsions are increasingly incorporating *Mimosa pudica* owing to its characteristics. These formulations enhance the therapeutic effects of plants by selectively targeting particular parts of the skin and prolonging the duration of contact. Given their convenient administration and enhanced drug penetration, emulgels are being increasingly employed for the treatment of localized skin conditions.[9] As the cosmetics sector adopts environmentally friendly practices, the significance of plant-based components is increasing. Although consumers desire environmentally friendly cosmetic products, the company also prioritizes environmental concerns. L'Oréal Group has committed to include 95% renewable plants or readily accessible minerals in their products by the year 2030. Extracts from the *Mimosa pudica* plant facilitate this transformation [6]. The ability to substitute petrochemical-derived components can effectively mitigate the environmental impact of cosmetics. Technological progress in extraction and green synthesis has enhanced the stability and bioavailability of plant-based medications. Nanoparticles derived from *Mimosa pudica* have been efficiently produced using green synthesis, resulting in enhanced bioactivity and novel applications in the field of cosmetics. Investigations have been conducted on the genus *Mimosa* to explore its potential in the production of nanoparticles of gold, silver, iron, cadmium, platinum, and zinc oxide. The enhanced stability and accurate targeting of these nanoparticles render them very suitable for use in cosmetics. Nevertheless, further study evaluating the efficacy of different *Mimosa* species is necessary to optimize their potential.[10] In the field of skincare, botanical cosmetics, which incorporate plant-derived components for both medicinal and cosmetic applications, will have a dominant position. In response to increasing awareness of the detrimental effects of synthetic chemicals, the beauty industry is developing safer alternatives derived from plants. Within this particular framework, *Mimosa pudica* presents a powerful combination of bioactive components for the purpose of natural and efficient skincare. With the increasing comprehension of the molecular mechanisms at play, *Mimosa pudica* will be included into a wider range of cosmetic products, so catering to consumers seeking natural skincare solutions and so promoting the sustainable beauty movement. The convergence of age-old medical expertise with contemporary beauty science presents fertile ground for innovation. A single compound can have anti-inflammatory, antibacterial, skin rejuvenating, and wound-healing properties, as demonstrated by *Mimosa pudica*.[20] The trajectory of the cosmetic industry hinges on botanical resources such as *Mimosa pudica*, driven by the increasing need for organic and environmentally sustainable beauty products.

MATERIALS AND METHODS

Geographic distribution, collection

Mimosa pudica is a plant that holds its profitable fame for broad-spectrum recognition in relation to the potential to flourish almost throughout, within most geographical regions around the world, in a huge range of environmental conditions. In India, it grows profusely in moist localities and covers the tropical and subtropical regions, since it is characterized by its humid climate condition.[6] This species goes well beyond the borders of India, and its distribution spreads over several countries in Asia: Bangladesh, Indonesia, Malaysia, Japan, Pakistan, Sri Lanka, China, Cambodia, and Taiwan. The adaptability of the plant allows it to grow in parts of Africa too, such as Nigeria, Mauritius, and Reunion Island, and it has established itself in regions of Australia as well. In America, it is widespread in countries like Brazil, Venezuela, Mexico, Cuba, northern Central America, Paraguay, Argentina, and Uruguay, where it has been adapted to both tropical and subtropical regions. Moreover, *Mimosa pudica* has spread to various Pacific Islands as well as Papua New Guinea and some areas of North America [10]. This wide distribution only underlines hardiness and variability in adaptation to different environmental conditions. It is extremely adaptable and grows in sensitive plants, with a variety of well-drained soils, even very degraded, eroded, or poor in nutrients. In this way, it is a species with colonizing capacity due to the resilience of the soil, which permits only plants with very low entries to establish tremendously in disturbed soils. They can spread extensively in pastures, especially in areas that experience frequent burning [13]. It is shade intolerant, usually not surviving shading by taller plants or on the floor of dense forests, hence it occurs in sunny and open places. An interesting feature of *Mimosa pudica* is that the plant emits carbon disulfide from its roots and acts as a self-protective agent by inhibiting mycorrhizal and pathogenic fungal colonization within the rhizosphere [14]. This special feature may give the plant an edge over its neighbors in the natural environment. The habitats of *Mimosa pudica* are also eclectic: croplands, orchards, pastures, mown lands, roadsides, and further anthropogenically disturbed landscapes from construction sites. The species can either grow as single plants or in tangled thickets spreading over vast areas. It commonly is found growing at altitudes from near sea level to about 1,300 meters and is adapted to areas with annual precipitations from 1,000 to more than 2,000 mm [15]. However, this plant being sensitive to frost, it can only be found limited in numbers in colder climates. Reproduction in *Mimosa pudica* is highly prodigious. In the Philippines, this plant flowers all year with as much as 675 seeds being produced by a single plant during a year [16]. This species is a wind and bee pollinated species, which enables it to spread over long distances. Seed is small, being air-dried seeds similar in weight from Puerto Rico averaged 0.0065 ± 0.0002 grams per seed [17]. They usually begin to germinate without pre treatment around 7 days after sowing and attain a peak of 17% in 94 days. However, proper pre treatment can almost exponentially increase the rates of germination. During one test, 80% of the seeds germinated in 4 weeks with treatment exposure to alternating temperatures of 20 and 40°C [15].

Bui's works presented an optimum treatment with warm water, and after that, the seeds were soaked with a view of obtaining the best germination [16]. The germination is epigeal, which means that during the process of germination, the cotyledons are hoisted above the soil. The seeds of *Mimosa pudica* are basically spread by means of a special mechanism developed with their pods: the bristles on the edges of their pods make them get entangled with clothing, animal fur, or feathers, thus enabling them to travel over long distances. Together with the high reproductive output of the plant, seed dispersal is successfully carried out, and this explains the fast spreading of the plant not only in the native but also in invaded ranges [17]. While seed propagation is the most common method adopted in nurseries and amateur plant cultivation, summer cuttings also work and hence form the other method that enthusiasts willing to cultivate the plant use. Its quite wide range of environmental adaptability, the diversity of reproductive strategy it is endowed with, and its great distribution make *Mimosa pudica* an exciting species for many perspectives in terms of potentiality for studies and applications not only in ecological management but also in horticulture practices. The fact that this plant naturally evolves to adapt to various climatic conditions, different soil types, and disturbances points out ecological resilience and justifies its widespread presence in several continents.[18]

Phytoconstituents

Table 2: Phytoconstituents present in *Mimosa pudica* Linn.

Phytochemical	Biological Activity	Localization	References
Alkaloids	Antimicrobial, Anti-inflammatory	Leaves	[19]
Flavonoids	Antioxidant, UV Protection	Seed & leaf extracts	[9]
Tannins	Astringent, Pore Tightening	Root	[16]
Glycosides	Skin Detoxification, Moisturization	Root	[8]
Terpenoids	Collagen Stimulation, Anti-Aging	Leaves	[6]
Phenolic Compounds	Hyperpigmentation Reduction	Leaf extract	[21]

Table 3: Types & Structure of Tannins

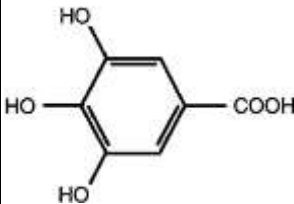
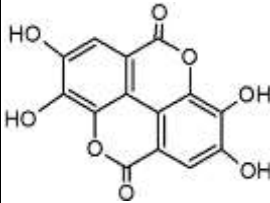
Tannins	Structure	References
Galic acid		[22],[23]
Ellagicacid		[9], [24]

Table 4: Types & Structure of Glycosides

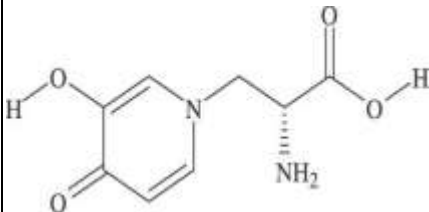
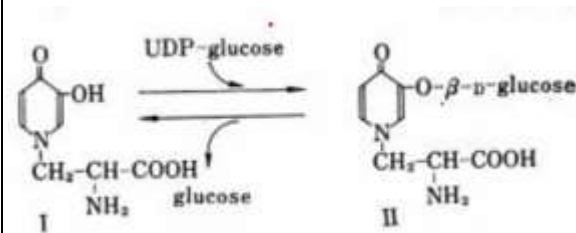
Glycosides	Structure	References
Mimosine		[25],[26]
Mimoside		[27]

Table 5: Types&StructureofTerpenoids

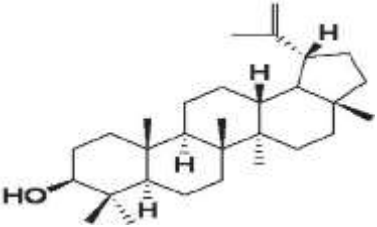
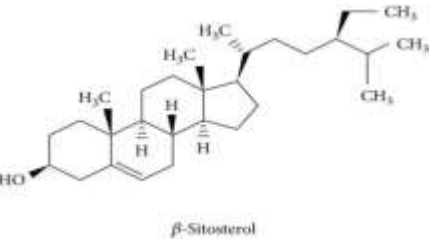
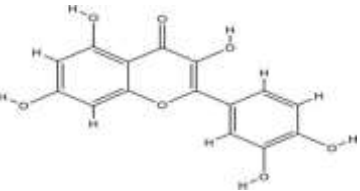
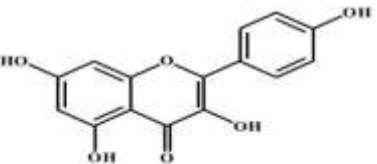
Terpenoids	Structure	References
Lupeol		[28],[29]
β -Sitosterol		[30],[31]

Table 6: Types & Structures of Phenolic Compounds

Phenolic Compounds	Structure	References
Quercetin		[32],[33]
Kaempferol		[34],[35]

Cosmetic application analysis

- **Antimicrobial activity**

The good diffusion method is a standard laboratory procedure followed for the determination of the efficacy of antimicrobial-capable agents. This test microorganism was specifically selected for the present study to determine the activity of *Mimosa pudica* against three particular test microbes: *Aspergillus fumigatus*, *Citrobacter divergence*, and *Klebsiella pneumoniae* because these microorganisms are significant in the causation of various infections, and resistance to some particular therapy. The extracts were tested at concentrations of 50 µg/disc, 100 µg/disc, and 200 µg/disc in the present investigation. The outcomes revealed that *Mimosa pudica* exhibited a significant effect against all the test microorganisms, but the sensitivity was dependent upon the concentration used. In general, bigger concentrations of *Mimosa pudica* produced a stronger inhibitory effect, thus pointing out its potential as a natural antimicrobial agent. The current study thus goes on to indicate the potential for *Mimosa pudica* in the contribution to the formulation of alternative treatments against such pathogenic infections. Of particular interest are its antimicrobial properties when used at high concentrations for developing new, plant-based solutions that will assist in overcoming microbial resistance and enhancing public health.[20]

- **Antioxidant activity**

The ethanolic extract of the plant *Mimosa pudica* belonging to the family Mimosaceae has been screened for its antioxidant activity using different standard assays such as DPPH, Nitric Oxide, ABTS, and Hydrogen peroxide free radicals. All the methods are currently recognized as the most widely used methods for determining substances that can neutralize free radicals and unstable molecules that play key roles in the initiation of tissues or cellular oxidative deterioration. The extract of *Mimosa pudica* revealed potent antioxidant activity in both the inhibition of Nitric Oxide and DPPH free radicals in these studies. The IC₅₀ value for Nitric Oxide was 78.1±1.75 µg/ml, while the value for DPPH was 35.00±1.15 µg/ml. From the above studies, the results obtained showed that the plant is regarded as a potent free radical scavenger. Thus, *Mimosa pudica* has substantial potential as a natural antioxidant that would be of benefit in safeguarding the body from oxidative stress and its related disorders.[20]

- **UV protection and sunscreen activity**

Some potential of *Mimosa pudica* as a natural sunscreen lies in its ability to protect the skin from damage caused by UV radiation. In this respect, it has been shown that 15% leaf extract of *Mimosa pudica* has an inhibitive action on the increase of tyrosinase enzyme activity and melanin production in UVB-induced guinea pigs. Tyrosinase is a rate-limiting enzyme for melanin biosynthesis, and its inhibition reduces pigmentation, thus helping to prevent UV-induced skin darkening and possible long-term damage. This protective action shows that *Mimosa pudica* may be useful in skin care products against harmful UV rays.

Mimosa pudica controls the uniform tone of skin color and sunspots, regulating the amount of melanin formation at the basal melanocytes and controlling, simultaneously, by regulating the activity of tyrosinase, an enzyme that stimulates melanin formation—the risk of sunspots, thus proving to be a great value for natural sunscreens and other UV protection formulations. [21]

PHARMACOLOGICAL ANALYSIS

- **Astringent properties**

1. **Pore tightening**

Mimosa pudica comes in pretty handy when dealing with tightening pores. It has tannins-natural compounds with extremely good astringent characteristics. So, how do tannins tighten the pores? The tannins cause coagulation of the proteins in the outer layer of the skin. This tightens and contracts the skin tissues in effect, making the pores visibly smaller. This will not only reduce the visibility of pores but also strengthen the natural barrier of the skin. As a result of this, it protects your skin more effectively from environmental toxins and impurities—two major culprits that bring about pore-clogging. With continued use over time, products containing Mimosa pudica will make your skin a lot smoother and even. This is not only cosmetically based but indeed is a result of its positive impact on the skin texture, offering a refined and youthful appearance. [20]

2. **Oil control**

But it doesn't stop here—Mimosa pudica also participates in the regulation of oil production. In its astringent properties lies a balancing action over sebum, the natural oil our skin produces. While sebum is crucial for keeping our skin both hydrated and protected, too much of it can be quite a nuisance and cause a greasy shine, and even lead to acne and other problems with the skin. This means that Mimosa pudica tightens the pores to reduce the amount of sebum reaching the skin surface. A balance in complexion is maintained, topped off by the minimization of shine and oiliness, especially in the forehead area, nose, and chin areas. Additionally, this plant reduces the risk of clogged pores and breakouts due to its ability to reduce the production of oil, thus resulting in clearer and healthier skin. [6]

- **Detoxifying agents**

1. **Skin detoxification**

Mimosa pudica is an herb very well known for its powerful detoxifying actions on the skin. The herb cleanses and purifies the body of impurities and toxins that naturally accumulate from exposure to air pollution, ultraviolet radiation, and even internal stressors. Unchecked, these can leave a lackluster, fatigued appearance and are potentially responsible for far more serious skin issues, including breakouts or early signs of aging. Integrated into skincare routines, Mimosa

pudica helps the skin to achieve its natural detoxification. This is a plant that gently yet efficiently cleanses subcutaneous impurities—hence, giving the skin an enhanced chance to breathe and renew itself without being disturbed. With time, such detoxifying action shall yield a much clearer complexion, leaving the skin vibrant, refreshed, and rejuvenated. Thus, detoxification goes in line with the maintenance of a balanced and healthy environment for the skin and is, therefore, crucial for long-term skin health. [8]

2. **Deep cleansing**

Other than the general detoxifying effects, *Mimosa pudica* is valued for its deep-cleansing properties. When included in facial cleansers, masks, or other skincare treatments, this plant will do way more than just wash away superficial dirt and oil off the skin. Instead, it goes deeper into the skin to a level where it breaks down stubborn impurities residing in the pores. The deep-cleansing action of *Mimosa pudica* is therefore crucial to preventing the settling of impurities that might block pores and cause disorders such as acne, blackheads, and dull skin. By effectively flushing deeply seated impurities, *Mimosa pudica* cleanses the skin from its core and turns it not only clean but deeply revitalized. This formulation of *Mimosa pudica* greatly improves the texture and appearance of skin with continued use. Skin begins to feel smoother, finer, and healthier-looking. Over time, this deep-cleansing action will underpin a complexion free from impurities and more resilient to negative environmental aggressors.[36]

• **Collagen induction**

1. **Better skin elasticity**

By promoting the production of collagen, *Mimosa pudica* is a vital regulator in skin elasticity and firmness. Collagen is responsible for giving structure to the skin, helping it to stay smooth and supple with resilience. Collagen is an important structural protein naturally found in our bodies. *Mimosa pudica* can offset the same by stimulating the skin to produce more of its own collagen.[37]

2. **Antiaging**

Apart from improved elasticity, it also makes the skin look much more toned and youthful. The hereby increased collagen level will make your skin hold its structure better and, therefore, diminishes appearance indications of fine lines and aging, holding the skin plump and healthy. This plant has a high anti-aging potential since it increases the production of collagen. Use of the skincare product infused with the plant continues to lessen the visible signs of aging, from sagging skin to uneven texture. *Mimosa pudica* is there to give way to wrinkles and fine lines, resulting in a refined, rejuvenated, and young complexion, leveling them flat on the skin by restoring skin elasticity and firmness. With time, regular consumption of a product-imposed form of it leaves one with an improved texture of the skin, firming up, and doing away with the sagging of the skin. Such is the use of *Mimosa pudica* in an anti-aging skin care routine, which

can cause an effect on skin protection that is both preventive and restorative in nature to retain youthful skin. [9]

- **Hyperpigmentation reduction**

1. **Even skin tone**

Mimosa pudica efficiently reduces the condition of hyperpigmentation and dark spots, thereby evening out your skin tone. Hyper-pigmentation is a condition wherein parts of a person's skin start to produce too much melanin, eventually forming darker patches. This happens due to excessive sun, aging process, or acne/cyst scars. Mimosa pudica inhibits the overproduction of melanin caused in certain areas of the skin and slowly lightens these dark spots, producing an even tone of skin. This botanical ingredient will help immensely in reducing the appearance of hyperpigmentation with regular use and make the skin tone more balanced and even.[21]

2. **Brightening effect**

Apart from evening out one's tone, Mimosa pudica also boasts a brightening effect. The herb reduces the zone of hyperpigmented areas, giving way to a brighter, radiant-looking glow. By evening out the rather uneven pigmentation, Mimosa pudica brightens up one's complexion so it looks vital and full of light. This brightening effect reduces dark spots and gives one a fresh, youthful look. Thus, Mimosa pudica becomes an asset in skincare products meant for clearer, brighter, and more radiant skin.[6]

DISCUSSION

- **Adverse effects**

Mimosa pudica has been reported to contain tannins, which exert astringent action on the skin, giving it a firm characteristic. However, with overuse, it leads to skin irritation, dry skin, and allergic reactions, which are to the disadvantage of a person with sensitive skin. An excessive amount of tannins can interfere with the natural barrier of the skin and lead thereafter to redness and flaking problems. [38]. They could also be cytotoxic. This cytotoxicity could result in the development of chronic skin damage, epidermal thinning, or reduction in cell turnover, and it may consequently compromise the ability of the skin to repair and regenerate.[38] While the antimicrobial activity of Mimosa pudica is beneficial in the prevention of infections, it definitely can disrupt the skin microbiome with overuse. This breakdown could predispose or exacerbate imbalances in skin bacteria, diseases like acne, rosacea, or other inflammatory skin conditions. Bioactive compounds in Mimosa pudica can trigger allergies in some people. This can turn up as contact dermatitis, with redness, itching, and sometimes swelling. The person with allergies to plants or sensitive skin should use it in caution. While Mimosa pudica is traditionally used in medicinal preparations, chronic or cosmetic use at high concentrations can lead to the

accumulation of toxins in the skin and adverse reactions, such as irritation, inflammation, or even systemic toxicity, very rarely.[19]

- **Homemade remedies**

Traditionally, either the crushed leaves of the plant were applied directly to wounds or skin irritations, promoting accelerated healing and suppressing inflammation, or other such uses were attributed to the anti-inflammatory and antibacterial nature of natural compounds found in the plant. In addition, *Mimosa pudica* is also used in skin home remedies for dark spots and hyperpigmentation because of its capacity to inhibit the "pro-melanogenesis" enzyme tyrosinase. Among the other uses of this plant are in the concoctions for bronchitis, piles, and other similar other ailments, thus proving quite versatile in home remedies. [39],[40],[41]

CONCLUSION

Mimosa pudica Linn is an herb that has a lot of potential use in the cosmetic industry because it has alkaloids, flavonoids, tannins, glycosides, terpenoids, and phenolic compounds. As far as the chosen high anti-inflammatory, antibacterial as well as antioxidant characteristics with UV protecting abilities are concerned it makes it very valuable. In anti-aging formulations, it is quite useful for skin care applications and has low side effects. This sets *Mimosa pudica* apart from many other herbs used in the botanical world, which can cause severe allergic reactions and even dermatitis. With *Mimosa pudica*, these side effects are non-existent; the plant only causes minor rashes or allergies. Therefore, this plant can be said to be a milder alternative to natural cosmetics because consumers increasingly demand completely natural emollient products. This aspect along with its ability to withstand different climate conditions also makes the plant highly sustainable and thus more attractive to the market making it an ideal ingredient for cosmeceuticals. The *mimosa pudica* plant has been found to be the best option for someone who wants to seek refuge in a safer and more natural way of solving skincare problems, hence ensuring customers' safety in line with meeting the high demand for eco-friendly products where the adverse effects are minimal.

Conflict of Interest:

There is no conflict of interest for preparing this manuscript.

Acknowledgement:

We sincerely express our gratitude to Dr. Adnan Shaikh, clinical pharmacist from Maitreya Multi Superspeciality Hospital, Surat. Guiding us for preparing this manuscript and providing a constant support and guidance throughout the preparation of manuscript.

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