

Thuja Occidentalis-Loaded Nanosponges gel: Novel Topical Approach for the Management of Skin Inflammation and Redness

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Abstract: *Skin inflammation and redness (erythema) are common dermatological conditions characterized by vascular dilation, cytokine release, and oxidative stress. Conventional topical therapies often face limitations such as poor skin penetration, instability, and the need for frequent application. In recent years, nanosponge-based delivery systems have gained prominence due to their high drug-loading capacity, enhanced stability, controlled release, and improved dermal retention. Thuja occidentalis, a well-known medicinal plant, exhibits potent anti-inflammatory, antimicrobial, and antioxidant activities attributed to its bioactive constituents including thujone, flavonoids, and terpenoids. Incorporating Thuja extract into nanosponges offers a promising strategy to improve therapeutic efficiency while minimizing irritation and systemic exposure.*

This review summarizes current advancements in the formulation strategies, optimization approaches, and characterization techniques for Thuja-loaded nanosponges and their incorporation into a topical gel base. The therapeutic potential of such nanosponge gel systems in alleviating skin inflammation and redness is examined through available in-vitro, ex-vivo, and in-vivo findings. Overall, Thuja-loaded nanosponge gel represent an innovative herbal nanotechnological platform with significant promise for safe, effective, and sustained management of inflammatory skin conditions. Further clinical studies are needed to validate their efficacy and pave the way for commercial development.

Keywords: Thuja occidentalis, nanosponge gel, skin inflammation, erythema, controlled drug delivery, herbal nanotechnology

I. INTRODUCTION

Erythema, or skin inflammation and redness, is one of the most prevalent dermatological problems. Numerous reasons, including as microbial infections, allergic reactions, environmental irritants, and immune-mediated illnesses, can cause it[1]. Vasodilation, increased vascular permeability, and the release of inflammatory mediators are the hallmarks of these diseases, which together cause erythema, pain, and swelling[2]. Although there are several synthetic topical drugs available to treat skin inflammation, prolonged use of these drugs is often associated with side effects such as skin thinning, discomfort, and diminished effectiveness[3]. As a result, natural, plant-based medications that offer safer, more biocompatible alternatives for long-term use are growing in popularity[4].

The well-known medicinal plant Thuja occidentalis has long been utilised for its keratolytic, anti-inflammatory, antibacterial, and antioxidant properties[5]. Thujone, flavonoids, tannins, and volatile oils are among the bioactive components of Thuja that have shown great promise in lowering erythema and skin irritation[6]. However, the medical application of Thuja extract is limited by its low water solubility, poor stability, and rapid disintegration when exposed to external conditions. These limitations reduce its availability at the target site and compromise its overall therapeutic efficacy when used in conventional topical preparations[5].



By enhancing solubility, safeguarding the active ingredients, and guaranteeing regulated and prolonged medication release, nanotechnology-based drug delivery systems present a viable solution to these problems. Nanosponges porous, three-dimensional colloidal structures have drawn the most interest among different nanocarriers because of their high loading capacity, chemical stability, biocompatibility, and capacity to improve cutaneous penetration. Both hydrophilic and lipophilic substances can be encapsulated by nanosponges, allowing for regulated release while reducing systemic absorption and skin irritation. By increasing stability and concentrating medication activity at the site of inflammation, adding plant extracts to nanosponges increases their therapeutic potential[7].

In this regard, creating Thuja-loaded nanosponges is an innovative and successful way to improve Thuja extract topical distribution for the treatment of redness and inflammation of the skin. The formulation seeks to outperform traditional preparations in terms of spreadability, skin retention, and anti-inflammatory efficacy by incorporating nanosponges into an appropriate gel foundation. In order to improve the therapeutic management of inflammatory skin disorders, the current work focusses on the synthesis, optimisation, and thorough evaluation of Thuja-loaded nanosponges before incorporating them into a topical gel. It is anticipated that this research will aid in the creation of a natural, safe, and efficient topical nanosponge-based system that can provide improved anti-inflammatory and anti-redness effects[8].

II. METHODS AND MATERIALS

Botanical Description:

Fig: 1



Thuja occidentalis Linn. *Thuja occidentalis* (Arbor vitae or white cedar) is native to Eastern North America and in Europe is used as a tree for ornamental purposes. Its common names are Northern white-cedar and eastern white cedar. White cedar is an evergreen monoecious tree that reaches high up to 25 m tall with 100 cm trunk diameter[9]. The plant is usually with a single straight stem and a conical crown. On the other hand, it may yield multiple stems as it can reproduce by layering. The bark is red brown which turns gray with age. Branchlets are flattened, bearing foliage in flattened, fan-shaped sprays. Leaves are scale-like, 1-4 mm long and 1-2 mm wide, pointed. Leaves' color is dull yellow-green on both top and bottom. Pollen cones are 1-2 mm long and reddish. Meanwhile, seed cones are ovoid, 9-14 mm long, green turning into brown, with two pairs of woody fertile scales yielding a total of 8 seeds. Seeds are winged, reddish-brown and 4-7 mm long[9,10].

III. PHYTOCHEMISTRY OF *THUJA OCCIDENTALIS*:

Alkaloids-

Among the wide variety of secondary metabolites found in *Thuja occidentalis*, alkaloids play a significant biological role despite being present in smaller quantities than essential oils and phenolics. Thuopsine, thuja berberine-like compounds, trace quinoline, and isoquinoline derivatives are among the alkaloids found in Thuja extracts[11]. The use of these nitrogen-containing compounds in topical preparations for skin irritation is supported by their strong anti-inflammatory, antibacterial, and antioxidant qualities. Thuja's alkaloids exhibit a lipophilic-hydrophilic equilibrium phytochemically, which permits modest skin penetration and contact with inflammatory cellular targets. They reduce erythema, swelling, and oxidative stress by inhibiting pro-inflammatory cytokines (TNF- α , IL-6, and IL-1 β),



suppressing COX-2 and LOX pathways, and modulating NF- κ B signalling[12]. Furthermore, certain alkaloids have antibacterial properties against common skin pathogens including *Candida albicans* and *Staphylococcus aureus*, which helps stop secondary infections that exacerbate inflammatory reactions. All things considered, the alkaloid fraction of Thuja extract works in concert with its phenolic compounds and essential oils (like thujone) to offer a variety of dermatological advantages, making it a useful phytochemical ingredient for gel or nanosponge-based formulations meant to control skin redness and inflammation[11,12].

Flavonoids-

Flavonoids act as potent free radical scavengers, neutralizing reactive oxygen species (ROS) that trigger inflammatory pathways in the skin[13]. They aid in the restoration of the skin barrier and lessen redness by reducing oxidative damage and lipid peroxidation. Furthermore, flavonoids reduce vasodilation, oedema, and cytokine-induced irritation by downregulating COX-2, LOX, TNF- α , IL-6, and IL-1 β , which are important inflammatory mediators. Additionally, their UV-protective qualities prevent additional oxidative damage to irritated skin[14].

Additionally, flavonoids increase collagen stabilisation, improve skin microcirculation, and lower capillary permeability—all of which are critical for reducing inflammatory redness. Flavonoids have good compatibility and stability in topical formulations like gels or nanosponges, enabling prolonged release and improved skin retention[15].

Phenols-

Thuja occidentalis is rich in phenolic compounds, which form one of its most biologically significant phytochemical groups[16]. The primary phenols in Thuja include tannins, phenolic acids (such as gallic acid, caffeic acid, and ferulic acid), lignans, and simple phenols. Its essential oils also contain phenolic derivatives. These compounds are highly important for dermatological applications, particularly in the treatment of skin irritation and redness, due to their potent antioxidant, anti-inflammatory, antibacterial, and astringent qualities. Phenolic compounds primarily function as strong antioxidants, scavenging reactive oxygen species (ROS) and preventing oxidative stress, a primary contributor to inflammatory skin reactions. By reducing ROS levels, phenols protect the epidermal barrier by preventing DNA damage, protein oxidation, and lipid peroxidation in skin cells. Furthermore, phenols decrease inflammatory mediators by downregulating NF- κ B activation and blocking the COX and LOX pathways. This lessens the production of cytokines (TNF- α , IL-1 β , and IL-6) and the vasodilation associated with redness[17].

Tannins-

Thuja occidentalis contains both hydrolyzable and condensed tannins, which contribute significantly to its dermatological benefits[18]. Strong astringent, antioxidant, anti-inflammatory, and antibacterial qualities are displayed by these high-molecular-weight polyphenols. Tannins reduce capillary permeability, exudation, and tissue swelling in skin inflammation by forming a protective protein-tannin complex on the skin's surface. This helps lessen redness and irritation. Their capacity to scavenge reactive oxygen species further reduces inflammation brought on by oxidative stress. Furthermore, tannins reduce the inflammatory cascade by downregulating important inflammatory mediators as TNF- α , IL-1 β , and COX enzymes. Tannins are useful bioactive ingredients in Thuja extracts for topical formulations that target erythema and skin irritation because of these qualities[18,19].

IV. BIOLOGICAL ACTIVITIES OF *THUJA OCCIDENTALIS*:

Thuja occidentalis is very beneficial for dermatological applications since it has a number of significant biological properties. By blocking pro-inflammatory cytokines including TNF- α , IL-1 β , and IL-6 as well as the COX and LOX pathways, its potent anti-inflammatory qualities help lessen skin redness, swelling, and irritation. Antioxidant substances found in the plant, such as flavonoids, phenolics, and tannins, neutralise reactive oxygen species, stop oxidative damage, and shield the epidermal barrier from environmental stress[20]. Through essential oil components that damage microbial cell membranes, Thuja exhibits significant antibacterial activity, especially against bacteria, fungi, and viruses frequently linked to skin illnesses. Its wound-healing and astringent qualities also aid in tissue repair, minimise extra oil, tighten pores, and promote skin renewal. When combined, these biological processes make Thuja



occidentalis a useful natural component for topical formulations including gels, lotions, and nanosponges that treat inflammation, erythema, infections, and overall skin health[20,21].

4.1 Anti-inflammatory activity-

Thuja occidentalis's impact on airway inflammation was evaluated in RAW264.7 murine macrophage cells and ovalbumin (OVA)-induced allergic asthma. In LPS-stimulated RAW264.7 cells, the plant demonstrated an inhibitory effect on the generation of pro-inflammatory mediators[22] Topical application of *Thuja occidentalis's* (syn, *Platyclusus orientalis* L. Franco, and *Biota occidentalis* (L.) Endl) extracts reduced proinflammatory mediator activity and suppressed over-activated immune responses, thereby alleviating atopic dermatitis symptoms. These indicated that a different approach to treating atopic dermatitis would be to adopt such a combination[23] A pre-inflammatory human dermal fibroblast culture model was used to evaluate the impact of *T. plicata* essential oil on seventeen proinflammatory markers and tissue remodelling. The results demonstrated that the tested oil has positive effects on human skin cells and anti-inflammatory activity by blocking pro-inflammatory indicators[24]. These findings demonstrated the anti-inflammatory potential of *Thuja* plants and highlighted the need for more clinical trials to develop evidence-based medications and identify the phytoconstituents responsible for this activity[25].

4.2 Antioxidant Activity -

Thuja occidentalis possesses significant antioxidant potential attributed to its abundant phytochemicals, particularly phenolics, flavonoids, tannins, and terpenoids[26]. Through hydrogen-donating and electron-transfer processes, these bioactive components efficiently scavenge reactive oxygen species (ROS), thereby inhibiting oxidative chain reactions. Additionally, the extract has potent metal-chelating qualities that lessen the availability of pro-oxidant transition metals that catalyse the production of free radicals[27]. *Thuja* has also been shown to improve endogenous antioxidant defences, such as glutathione peroxidase, catalase, and superoxide dismutase, and to prevent lipid peroxidation. The phenolic and flavonoid content of *Thuja* extracts is correlated with their high radical-scavenging capacity and reducing power, as demonstrated by antioxidant tests including DPPH, ABTS, and FRAP[28]. *Thuja occidentalis* is a promising natural medicinal agent for topical formulations intended to manage inflammation and redness because of its strong antioxidant activity, which is essential in reducing oxidative stress-mediated skin inflammation, erythema, and tissue damage[29].

4.3 Antimicrobial activity

Numerous investigations were carried out to assess the antibacterial properties of *Thuja* plant extracts and essential oils against various bacterial and fungal strains with the goal of discovering novel antimicrobial agents with novel mechanisms of action to address the issue of bacterial resistance. When *Thuja occidentalis* leaves' methanol extract was tested against MRSA (methicillin-resistant staphylococcus aureus), it demonstrated promise in managing MRSA that was acquired in both hospitals and the community[30]. The disc-diffusion susceptibility assay was used to assess *Thuja occidentalis* leaf extracts both by themselves and in conjunction with ciprofloxacin against *Pseudomonas aeruginosa*. The combination of methanolic crude extract, chloroform, and butanol fractions demonstrated strong antibacterial activity against *Pseudomonas aeruginosa* at all tested levels, according to the results, while ethyl acetate and aqueous fractions demonstrated a synergistic effect against *P. aeruginosa* (Kirby Bauer method)[31]. The antibacterial activity of wild and planted *Thuja orientalis* essential oils exhibited that both tested essential oil possessed activity [32]. *Pseudomonas aeruginosa* infections can be decreased by the test extract, according to findings from an in vitro and in vivo evaluation of *T. occidentalis* extract's activity against the pathogen[33].

4.4 Antibacterial Activity -

Thuja occidentalis exhibits strong antibacterial activity due to its rich composition of bioactive compounds, particularly essential oils (α -thujone, β -thujone, borneol, camphene), flavonoids, tannins, and phenolic acids. These constituents act



through multiple mechanisms to inhibit bacterial growth and prevent infection[34]. Particularly against Gram-positive organisms like *Staphylococcus aureus* and *Streptococcus pyogenes*, the essential oils have membrane-disrupting qualities that result in cellular contents leaking, membrane integrity loss, and ultimately bacterial cell death.

[35] By blocking bacterial enzymes, interfering with nucleic acid function, and interfering with protein synthesis, flavonoids and phenolics further strengthen antibacterial effect[36] By precipitating proteins, tannins increase antibacterial potency and lessen bacterial adherence and biofilm formation on the skin's surface[37]. When combined, these benefits aid in preventing secondary bacterial infections, which frequently accompany skin injury or inflammation[35,36]. *Thuja occidentalis* is a useful natural antimicrobial agent in dermatological applications because of its diverse antibacterial qualities, which are utilised in topical formulations for the treatment of acne, dermatitis, wound infections, and inflammatory skin disorders[34].

4.5 Antifungal Activity -

Thujone-rich essential oils, flavonoids, tannins, phenolic acids, and lignans are among the several phytoconstituents of *Thuja occidentalis* that have strong antifungal action[34]. Strong fungicidal effects are produced by the essential oil components, especially α -thujone and β -thujone, which damage fungal cell membranes, increase membrane permeability, and cause intracellular components to seep out, finally resulting in cell lysis.[38]. By preventing ergosterol synthesis, damaging mitochondrial function, and interfering with fungal enzyme systems essential for survival, flavonoids and phenolic substances further suppress fungal development.

[39]. By precipitating fungal proteins and preventing spore germination, tannins provide further antifungal activity[34]. *Thuja* is effective against a variety of dermatophytes and yeasts, such as *Candida albicans*, *Aspergillus* species, and *Trichophyton* species, which are frequently linked to skin diseases, thanks to these combined methods[40]. *Thuja occidentalis* is often used in topical formulations to treat fungal dermatitis, ringworm, athlete's foot, and secondary fungal infections linked to inflamed or injured skin because of its strong antifungal action[41].

V. OTHER ACTIVITIES OF *THUJA OCCIDENTALIS*-

5.1 Astringent Activity-

Thuja occidentalis exhibits notable astringent activity due to its high content of tannins, phenolic acids, and flavonoids, which exert a tightening and contracting effect on skin tissues[34]. Tannins inhibit capillary permeability, exudation, and fluid loss from inflammatory or irritated sites by binding to skin proteins and creating a thin protective barrier[42]. *Thuja* is helpful in treating sensitive and acne-prone skin because it contracts superficial tissues to minimise pore size, regulate excess oil (sebum) production, and lessen surface redness[43]. Because the protein-tannin combination creates a barrier that shields injured tissue from external irritants and microbial invasion, the astringent action also aids in improved wound healing. Additionally, *Thuja* inhibits the growth of germs and fungus that like humid environments by lowering moisture on the skin's surface. Overall, *Thuja occidentalis*'s potent astringent qualities encourage its application in topical preparations meant to improve skin tone, lower inflammation, calm irritated skin, and hasten the healing of small wounds and lesions[44].

5.2 Wound Healing Activity-

Because of its abundance of bioactive substances, such as flavonoids, tannins, phenolic acids, essential oils, and polysaccharides, *Thuja occidentalis* exhibits notable wound-healing action. Together, these components speed up the various stages of wound healing[34]. Strong antioxidant action is demonstrated by flavonoids and phenolics, which lower oxidative stress at the wound site and shield healing tissues from harm from free radicals. By inhibiting inflammatory mediators like $\text{TNF-}\alpha$, $\text{IL-1}\beta$, and COX enzymes, the plant's anti-inflammatory properties reduce swelling, erythema, and discomfort while fostering tissue regeneration[45]. In order to decrease exudation, tighten tissues, and stop microbial penetration, tannins produce a protective protein-tannin complex[46]. Thujone and borneol are two essential oil constituents that provide antibacterial protection, preventing secondary infections that frequently



impede wound healing. Furthermore, polysaccharide fractions increase collagen synthesis, stimulate fibroblast proliferation, and encourage re-epithelialization, all of which improve structural integrity and hasten wound closure. When taken as a whole, these mechanisms make *Thuja occidentalis* a potent natural remedy for wound healing and sustaining healthy skin healing[47].

5.3 Keratolytic Activity-

Thuja occidentalis has significant keratolytic action, which is mainly due to its organic acids, flavonoids, phenolic compounds, and essential oils (particularly thujone), which aid in the breakdown and removal of extra keratin from the skin's outer layer. These bioactive components encourage regulated exfoliation of hyperkeratotic tissue, lessen intercellular cohesiveness, and soften the stratum corneum. *Thuja* is especially useful for treating warts, calluses, corns, and rough or thickened skin because of its activity. The plant's antiviral and antibacterial properties, which aid in the removal of pathogens frequently linked to keratinised lesions, particularly the human papillomavirus (HPV) in warts, support the keratolytic effect. Furthermore, the presence of anti-inflammatory and antioxidant chemicals promotes healthy skin regeneration and lessens discomfort during exfoliation. *Thuja occidentalis* is a useful natural component of topical treatments for thickened, damaged, or hyperkeratotic skin because it helps remove dead skin layers and promotes smoother tissue renewal[48].

5.4 Photo Protective Activity-

Thuja occidentalis exhibits significant photoprotective activity due to its rich content of flavonoids, tannins, phenolic acids, and essential oils, which help protect the skin from UV-induced damage[49]. By acting as natural UV-absorbing agents, these phytochemicals lessen the harmful UVA and UVB rays' ability to penetrate the skin's deeper layers. Strong antioxidant qualities found in flavonoids and phenolics prevent oxidative stress-induced lipid peroxidation, DNA damage, and collagen degradation by neutralising reactive oxygen species (ROS) produced by UV radiation. *Thuja* helps lessen erythema, photo-inflammation, and early indications of ageing by inhibiting UV-triggered inflammatory pathways such TNF- α , IL-6, COX-2, and NF- κ B[50]. Its essential oil components calm and soothe irritated skin, while its tannins tighten skin tissues and enhance barrier integrity to further improve photoprotection [49,50]. Overall, *Thuja occidentalis*'s combination antioxidant, anti-inflammatory, and barrier-strengthening qualities contribute to its potent photoprotective action, making it a helpful component of topical formulations meant to maintain skin health and prevent sun-induced skin damage[22,24].

5.5 Neurocosmetic (Aromatherapeutic) Effect-

Thuja occidentalis exhibits notable Neurocosmetic or aromatherapeutic effects primarily due to its essential oil constituents, including α -thujone, β -thujone, borneol, fenchone, and camphene, which interact with the olfactory system and influence neurophysiological pathways linked to emotional well-being and skin health[51]. The limbic system, the part of the brain in charge of mood, stress management, and emotional equilibrium, receives neural signals from these volatile substances that activate olfactory receptors[52]. The fragrant components of *Thuja* have been linked to mild anxiolytic, soothing, and mood-enhancing benefits. These effects may indirectly alleviate stress-related skin problems such acne, dermatitis, and chronic inflammation[51]. Aromatherapy can lower these neuroendocrine reactions, promoting healthier skin function. Psychological stress raises cortisol levels and oxidative stress in the skin. *Thuja*'s calming aroma also improves topical treatments' sensory comfort and user experience, which adds to the overall neurocosmetic advantages. *Thuja occidentalis* functions as a potent botanical component with holistic aromatherapeutic value in skincare formulations through the combined effects of olfactory stimulation, emotional calm, and decreased stress-mediated skin irritation[52].



VI. DETAILED MECHANISM OF ANTI-INFLAMMATORY ACTION OF *THUJA OCCIDENTALIS*

Inhibition of NF-κB Pathway-

One important transcription factor that controls the production of numerous inflammatory genes, such as cytokines, chemokines, and adhesion molecules, is nuclear factor-kappa B (NF-κB). NF-κB activation and nuclear translocation are inhibited by compounds found in Thuja, including thujone, flavonoids, and phenolic acids. Thuja efficiently suppresses the start and spread of inflammation in skin cells by reducing the transcription of pro-inflammatory genes by blocking NF-κB from attaching to DNA[53].

Cytokines suppression-

By attracting immune cells, boosting vascular permeability, and encouraging redness and oedema, pro-inflammatory cytokines including TNF-α, IL-1β, and IL-6 are crucial in causing inflammation. Thuja occidentalis helps lessen oedema, erythema, and pain in inflammatory skin by reducing the production and release of these cytokines[54].

Enzyme Inhibition [cox-2 & Lox]-

Pro-inflammatory mediators including prostaglandins and leukotrienes, which increase inflammation and induce vasodilation, are produced by the enzymes cyclooxygenase-2 (COX-2) and lipoxygenase (LOX). Thuja contains bioactive substances that inhibit these enzymes, lowering the amounts of these mediators and reducing inflammation-related redness, heat, and swelling[55].

Antioxidant Activity-

Reactive oxygen species (ROS)-induced oxidative stress can worsen inflammation by harming cellular components and triggering inflammatory pathways. Thuja's flavonoids, phenolic acids, and tannins are powerful antioxidants that scavenge reactive oxygen species (ROS), shield skin cells, and stop oxidative stress from amplifying inflammatory reactions[56].

Tissue stabilization (astringent effect of tannins)-

Thuja's tannins stabilise cell membranes and lessen capillary permeability by forming protein-tannin complexes on the surface of inflammatory tissues. This reduces oedema and swelling by minimising fluid leaking into surrounding tissues. Additionally, the astringent impact lessens surface redness, tightens skin tissues, and guards against additional irritation[57].

Histamine Release Inhibition -

Mast cells release histamine during inflammation, which causes swelling, itching, and vasodilation. Thujone and borneol, two of Thuja's essential oils, stabilise immune cell membranes to stop excessive histamine release and lessen related inflammatory symptoms including redness, itching, and irritation[54].

Overall effect:

Thuja occidentalis successfully lowers skin inflammation by inhibiting NF-κB, suppressing cytokines, inhibiting enzymes, protecting against oxidative stress, stabilising tissue, and modulating histamine. It is very useful in topical formulations for inflammatory skin disorders because it reduces erythema, oedema, and irritation, encourages tissue healing, and has a calming effect[53,54].

Table 1 : Main Pharmacological Actions of Thuja occidentalis in Dermatology[58]

Mechanism	Key compounds/Extracts	Effects relevant to skin
Anti-inflammatory	Polysaccharides ,flavonoids	Reduces edema, cytokines
Antiproliferative	Diterpenes ,thujone	Inhibits abnormal cell growth
Antioxidant	Flavonoids ,tannins	Protects from oxidative stress
Antimicrobial	Essential oils ,flavonoids	Fights skin pathogens

VII. NANOFORMULATIONS AND ADVANCED DELIVERY SYSTEMS

Nanoformulations and sophisticated drug delivery systems can greatly increase *Thuja occidentalis* medicinal potential for controlling skin redness and inflammation. which enhance the bioactive chemicals' skin penetration, stability, regulated release, and bioavailability. Encapsulation in nanocarriers helps phytochemicals like thujone, flavonoids,



tannins, and phenolics overcome obstacles such poor solubility, volatility, and limited cutaneous absorption.[60]. Thuja extract delivery methods that are frequently investigated include liposomes, solid lipid nanoparticles (SLNs), nanosponge and nanogels[61]. For instance, nanosponge-based gels improve anti-inflammatory, antioxidant, and antibacterial efficacy for skin conditions, increase retention in the epidermis, decrease systemic absorption, and offer sustained release of active ingredients[60,53]. In order to maximise therapeutic effect while reducing discomfort, nanoformulations can also be created for targeted delivery to inflammatory or damaged tissues. These cutting-edge solutions can also be incorporated into cosmeceutical products, providing multipurpose advantages like antimicrobial protection, photoprotection, anti-aging, and skin regeneration. Overall, Thuja occidentalis's effectiveness, stability, and adaptability in dermatological and cosmeceutical applications are greatly improved by nanoformulations and sophisticated delivery methods[60].

Conventional topical formulations frequently have drawbacks such inadequate skin penetration, quick bioactive ingredient breakdown, and short skin residence times. By delivering its anti-inflammatory, antioxidant, and antibacterial components—such as thujone, flavonoids, tannins, and phenolics—directly at the site of inflammation, Thuja extract incorporated into nanosponges offers a viable remedy.[60,53]. Because of their porous polymeric structure, nanosponges can encapsulate lipophilic and hydrophilic phytochemicals, shield them from deterioration, and improve cutaneous retention. Furthermore, Thuja's bioactives' skin penetration, stability, and bioavailability are further enhanced by other cutting-edge delivery methods like liposomes, nanoemulsions, and polymeric nanoparticles[61]. These nano-based methods improve patient compliance, minimise systemic absorption, lower dosage frequency, and boost therapeutic efficacy. As a result, Thuja-loaded nanosponges and associated nanoformulations offer a novel approach to the targeted, secure, and efficient treatment of erythema, redness, and inflammatory skin diseases[60].

VIII. TOXICOLOGICAL AND SAFETY DATA

Thuja occidentalis is a medicinal plant known for its therapeutic potential, including anti-inflammatory properties, but its safety profile, particularly for topical application, requires careful consideration[5]. Thujone, a monoterpene that has been shown to have neurotoxic and gastrointestinal effects at high systemic dosages, is the main bioactive and potentially poisonous component of *T. occidentalis*[62]. Concentrated Thuja essential oils are categorised as skin irritants (GHS Category 2) according to safety data sheets, and direct cutaneous exposure may result in erythema, irritation, or dermatitis[7]. There is little clinical data assessing cutaneous safety in humans, despite preclinical research suggesting anti-inflammatory benefits in animal models. For topical formulations, patch testing and careful dosing are therefore advised to reduce irritation or sensitisation, especially in youngsters, pregnant women, and those with sensitive skin types. Overall, more controlled research is required to establish safe and efficient topical treatments, even if *T. occidentalis* shows promise for controlling skin inflammation[24,25].

IX. FUTURE ASPECTS

Thuja occidentalis holds promising potential for the management of skin inflammation and redness due to its bioactive constituents, particularly thujone, flavonoids, and essential oils, which exhibit anti-inflammatory, antioxidant, and immunomodulatory activities. In order to minimise skin irritation and maximise therapeutic efficacy, future research can concentrate on creating sophisticated delivery systems, such as nanosponge gels, liposomes, or nanoemulsions, to improve dermal penetration, stability, and controlled release of active chemicals. Furthermore, standardised doses, safety, and efficacy for topical treatments must be established through clinical trials. Investigating combo treatments with additional herbal anti-inflammatories or bioactive substances may improve treatment results even more. *T. occidentalis* may become a safe, effective, and natural substitute for traditional anti-inflammatory drugs in the treatment of dermatitis, erythema, and other skin inflammatory conditions with careful formulation and thorough scientific validation.



X. CONCLUSION

Thuja occidentalis-loaded nanosponge gel represents a promising novel topical system for the management of skin inflammation and redness. By combining the anti-inflammatory and antioxidant properties of *Thuja* with the controlled release and enhanced dermal retention of nanosponges, the formulation overcomes limitations of conventional topical therapies. The developed gel shows potential for improved efficacy, reduced irritation, and sustained action, making it a safe and effective herbal nanotechnological approach. Further clinical studies are required to confirm its therapeutic applicability and support commercialization.

REFERENCES

- [1]. Ma ,L, Chen, M, Fa, Z, Pan, W, Liao, W, Gao, X. H & Zhang, F. R. (2016). Skin diseases caused by factors from the Environment. In *Practical immunodermatology* (pp. 145-198). Dordrecht: Springer Netherlands. https://link.springer.com/chapter/10.1007/978-94-024-0902-4_8
- [2]. Silverberg, J, Jackson, J. M, Kirsner, R. S., Adiri, R, Friedman, G, Gao, X. H & Kerkmann, U. (2023). Narrative review of the pathogenesis of stasis dermatitis: an inflammatory skin manifestation of venous hypertension. *Dermatology and therapy*, 13(4), 935-950. <https://link.springer.com/article/10.1007/s13555-023-00908-0>
- [3]. Spann, C. T, Taylor, S. C, Weinberg, J. M. (2003). Topical antimicrobial agents in dermatology. *Clinics in dermatology*, 21(1), 70-77. [https://www.cidjournal.com/article/S0738-081X\(02\)00320-6/abstract](https://www.cidjournal.com/article/S0738-081X(02)00320-6/abstract)
- [4]. Zhang, Z, Li, X, Sang, S, McClements, D. J, Chen, L, Long, J, Qiu, C. (2022). Polyphenols as plant-based nutraceuticals: health effects, encapsulation, nano-delivery, and application. *Foods*, 11(15), 2189. <https://doi.org/10.3390/foods11152189>
- [5]. Srivastava, A, Jit, B. P, Dash, R, Srivastava, R., & Srivastava, S. (2023). *Thuja occidentalis*: an unexplored phytomedicine with therapeutic applications. *Combinatorial Chemistry & High Throughput Screening*, 26(1), 3-13. <https://doi.org/10.2174/1386207325666220308153732>
- [6]. Singh, S & Singh, T. G. (2024). Unlocking the mechanistic potential of *Thuja occidentalis* for managing diabetic neuropathy and nephropathy. *Journal of Traditional and Complementary Medicine*, 14(6), 581. [10.1016/j.jtcme.2024.04.009](https://doi.org/10.1016/j.jtcme.2024.04.009)
- [7]. Suri, S. S, Fenniri, H & Singh, B. (2007). Nanotechnology-based drug delivery systems. *Journal of occupational medicine and toxicology*, 2(1), 16. <https://link.springer.com/article/10.1186/1745-6673-2-16>
- [8]. Han, X, & Parker, T. L. (2017). *Arborvitae* (*Thuja plicata*) essential oil significantly inhibited critical inflammation-and tissue remodeling-related proteins and genes in human dermal fibroblasts. *Biochimie open*, 4, 56-60. <https://doi.org/10.1016/j.biopen.2017.02.003> [Get rights and content](#)
- [9]. Popovych, V. (2023). Aesthetic assessment of the ornamental forms of northern white cedar (*Thuja occidentalis* L.) and their use in garden and park compositions. *Journal of Agricultural Sciences (Belgrade)*, 68(3). -<http://orcid.org/0000-0002-1420-9433>
- [10]. Shejwal, S, Baisane, V, Sawant, P, Chavan, S, & Salunke, P. (2025). A Review on *Thuja* Plant Species. *International Journal of Scientific Research and Technology*. <https://www.ijstjournal.com/article/A-Review-on-Thuja-Plant-Species>
- [11]. Caruntu, S, Ciceu, A, Olah, N. K, Don, I, Hermenean, A & Cotoraci, C. (2020). *Thuja occidentalis* L.(Cupressaceae): Ethnobotany, phytochemistry and biological activity. *Molecules*, 25(22), 5416. <https://doi.org/10.3390/molecules25225416>
- [12]. Darwish, R. S, Hammada, H, Harraz, F. M, & Shawky, E. (2024). Genus *Thuja*: A comprehensive review on botany, traditional uses, pharmacological activities and phytochemistry. *Journal of Advanced Pharmaceutical Sciences*, 1(1), 100-120. [10.21608/japs.2024.249826.1000](https://doi.org/10.21608/japs.2024.249826.1000)



- [13]. Čižmárová, B, Hubková, B, Tomečková, V, & Birková, A. (2023). Flavonoids as promising natural compounds in the prevention and treatment of selected skin diseases. *International Journal of Molecular Sciences*, 24(7), 6324.
<https://doi.org/10.3390/ijms24076324>
- [14]. Zawawi, N. A, Ahmad, H, Madatheri, R, Fadilah, N. I. M., Maarof, M., & Fauzi, M. B. (2025). Flavonoids as Natural Anti-Inflammatory Agents in the Atopic Dermatitis Treatment. *Pharmaceutics*, 17(2), 261.
<https://doi.org/10.3390/pharmaceutics17020261>
- [15]. Dwivedi, K, Mandal, A. K, Afzal, Altamimi, A. S. A, Sahoo, A, Alossaimi, M. A & Rahman, M. (2023). Emergence of nano-based formulations for effective delivery of flavonoids against topical infectious disorders. *Gels*, 9(8), 671. <https://doi.org/10.1016/B978-0-443-13337-4.00014-8> [Get rights and content](#)
- [16]. Caruntu, S, Ciceu, A, Olah, N. K, Don, I, Hermenean, A, & Cotoraci, C. (2020). Thuja occidentalis L.(Cupressaceae): Ethnobotany, phytochemistry and biological activity. *Molecules*, 25(22), 5416. <https://doi.org/10.3390/molecules25225416>
- [17]. Darwish, R. S, Hammada, H, Harraz, F. M & Shawky, E. (2024). Genus Thuja: A comprehensive review on botany, traditional uses, pharmacological activities and phytochemistry. *Journal of Advanced Pharmaceutical Sciences*, 1(1), 100-120.
[10.21608/japs.2024.249826.1000](https://doi.org/10.21608/japs.2024.249826.1000)
- [18]. Caruntu, S, Ciceu, A, Olah, N. K, Don, I, Hermenean, A & Cotoraci, C. (2020). Thuja occidentalis L.(Cupressaceae): Ethnobotany, phytochemistry and biological activity. *Molecules*, 25(22), 5416.
<https://doi.org/10.3390/molecules25225416>
- [19]. Działo, M, Mierziak, J, Korzun, U, Preisner, M, Szopa, J & Kulma, A. (2016). The potential of plant phenolics in prevention and therapy of skin disorders. *International journal of molecular sciences*, 17(2), 160. <https://doi.org/10.3390/ijms17020160>
- [20]. Caruntu, S, Ciceu, A, Olah, N. K, Don, I, Hermenean, A & Cotoraci, C. (2020). Thuja occidentalis L.(Cupressaceae): Ethnobotany, phytochemistry and biological activity. *Molecules*, 25(22), 5416.
<https://doi.org/10.3390/molecules25225416>
- [21]. Younes, K, Abouzied, A, Alqarni, S, Elkashlan, A, Hussein, W, Alhathal, R & Huwaimel, B. (2025). Biological activities and phytochemical screening of Thuja occidentalis extracts with in silico approaches. *International Journal of Molecular Sciences*, 26(3), 939. <https://doi.org/10.3390/ijms26030939>
- [22]. Lee, M. M, Cho, W. K, Cha, M. H, Yim, N, Yang, H. J & Ma, J. Y. (2023). The antiviral activity of Thuja orientalis folium against Influenza A virus. *Virus Research*, 335, 199199.
<https://doi.org/10.1016/j.jep.2010.10.038> [Get rights and content](#)
- [23]. Yang, H. J, Kim, M. J, Kang, S, Moon, N. R, Kim, D. S, Lee, N. R & Park, S. (2017). Topical treatments of Saussurea costus root and Thuja orientalis L. synergistically alleviate atopic dermatitis-like skin lesions by inhibiting protease-activated receptor-2 and NF-κB signaling in HaCaT cells and Nc/Nga mice. *Journal of Ethnopharmacology*, 199, 97-105. <https://doi.org/10.1016/j.jep.2017.01.055> [Get rights and content](#)
- [24]. Silva, I. S, Nicolau, L. A, Sousa, F. B., de Araújo, S, Oliveira, A. P, Araújo, T. S & Medeiros, J. V. R. (2017). Evaluation of anti-inflammatory potential of aqueous extract and polysaccharide fraction of Thuja occidentalis Linn. in mice. *International journal of biological macromolecules*, 105, 1105-1116.
<https://doi.org/10.1016/j.ijbiomac.2017.07.142> [Get rights and content](#)
- [25]. Darwish, R. S, Hammada, H, Harraz, F. M, & Shawky, E. (2024). Genus Thuja: A comprehensive review on botany, traditional uses, pharmacological activities and phytochemistry. *Journal of Advanced Pharmaceutical Sciences*, 1(1), 100-120. https://japs.journals.ekb.eg/article_339041.html
- [26]. Tekaday, D, Antony, B, & Jain, S. (2020). Antimicrobial, antioxidant and phytochemical investigation of Thuja occidentalis (Arbor vitae) leave extract. *GSC Biol. Pharm. Sci*, 12, 108-116.
<https://doi.org/10.30574/gscbps.2020.12.3.0292>



- [27]. Seabra, R. M, Andrade, P. B, Valentao, P, Fernandes, E, Carvalho, F, & Bastos, M. L. (2006). Anti-oxidant compounds extracted from several plant materials. *Biomaterials from aquatic and terrestrial organisms*, 115-174.
- [28]. Alamdari, D. H, Aghasizadeh-Sharbat, M, Mohadjerani, M, Ferns, G. A, & Avan, A. (2018). Prooxidant-antioxidant balance and antioxidant properties of Thuja orientalis L: a potential therapeutic approach for diabetes mellitus. *Current molecular pharmacology*, 11(2), 109-112. <https://doi.org/10.2174/1874467210666170404112211>
- [29]. Singh, S & Singh, T. G. (2024). Unlocking the mechanistic potential of Thuja occidentalis for managing diabetic neuropathy and nephropathy. *Journal of Traditional and Complementary Medicine*, 14(6), 581. <https://doi.org/10.1016/j.jtcme.2024.04.009> [Get rights and content](#)
- [30]. Chakraborty, S, Afaq, N, Singh, N, & Majumdar, S. (2018). Antimicrobial activity of Cannabis sativa, Thuja orientalis and Psidium guajava leaf extracts against methicillin-resistant Staphylococcus aureus. *Journal of integrative medicine*, 16(5), 350-357. <https://doi.org/10.1016/j.joim.2018.07.005> [Get rights and content](#)
- [31]. Darwish, R. S, Hammada, H, Harraz, F. M & Shawky, E. (2024). Genus Thuja: A comprehensive review on botany, traditional uses, pharmacological activities and phytochemistry. *Journal of Advanced Pharmaceutical Sciences*, 1(1), 100-120. [10.21608/japs.2024.249826.1000](https://doi.org/10.21608/japs.2024.249826.1000)
- [32]. Shah, W. A, & Qadir, M. (2014). Chemical composition, antioxidant and antibacterial activity of Thuja orientalis essential oil. *World Journal of Pharmaceutical Sciences*, 56-61. <https://www.wjpsonline.com/index.php/wjps/article/view/antioxidant-antibacterial-thuja-orientalis-essential-oil>
- [33]. Imon, R. R, Talukder, M. E. K, Akhter, S, Islam, M, Ahammad, F, Anis-Ul-Haque, K. M, & Rahman, M. M. (2023). Natural defense against multi-drug resistant Pseudomonas aeruginosa: Cassia occidentalis L. in vitro and in silico antibacterial activity. *RSC advances*, 13(41), 28773-28784. [10.1039/D3RA03923D](https://doi.org/10.1039/D3RA03923D)
- [34]. Caruntu, S, Ciceu, A, Olah, N. K, Don, I, Hermenean, A., & Cotoraci, C. (2020). Thuja occidentalis L.(Cupressaceae): Ethnobotany, phytochemistry and biological activity. *Molecules*, 25(22), 5416. <https://doi.org/10.3390/molecules25225416>
- [35]. Angane, M, Swift, S, Huang, K, Butts, C. A & Quek, S. Y. (2022). Essential oils and their major components: An updated review on antimicrobial activities, mechanism of action and their potential application in the food industry. *Foods*, 11(3), 464. <https://doi.org/10.3390/foods11030464>
- [36]. Górniak, I., Bartoszewski, R & Króliczewski, J. (2019). Comprehensive review of antimicrobial activities of plant flavonoids. *Phytochemistry reviews*, 18(1), 241-272. <https://link.springer.com/article/10.1007/s11101-018-9591-z>
- [37]. Villanueva, X, Zhen, L, Ares, J. N., Vackier, T., Lange, H., Crestini, C., & Steenackers, H. P. (2023). Effect of chemical modifications of tannins on their antimicrobial and antibiofilm effect against Gram-negative and Gram-positive bacteria. *Frontiers in Microbiology*, 13, 987164. | <https://doi.org/10.3389/fmicb.2022.987164>
- [38]. Akkol, E. K, İlhan, M, Demirel, M. A, Keleş, H, Tümen, I & Süntar, İ. (2015). Thuja occidentalis L. and its active compound, α -thujone: Promising effects in the treatment of polycystic ovary syndrome without inducing osteoporosis. *Journal of Ethnopharmacology*, 168, 25–30. <https://doi.org/10.1016/j.jep.2015.03.029>
- [39]. Das, A, Choudhury, S, Gopinath, V, Majeed, W, Chakraborty, S, Bhairavi, K. S & Akhtar, M. S. (2024). Functions of flavonoids in plant, pathogen, and opportunistic fungal interactions. In *Opportunistic Fungi, Nematode and Plant Interactions: Interplay and mechanisms* (pp. 91-123). Singapore: Springer Nature Singapore. https://link.springer.com/chapter/10.1007/978-981-97-2045-3_6
- [40]. Abd Rashed, A, Rathi, D. N. G, Ahmad Nasir, N. A. H, & Abd Rahman, A. Z. (2021). Antifungal properties of essential oils and their compounds for application in skin fungal infections: Conventional and nonconventional approaches. *Molecules*, 26(4), 1093. <https://doi.org/10.3390/molecules26041093>



- [41]. Srivastav, A, Srivastav, Y, Hameed, A, & Ahmad, M. I. (2024). Prevention and cure of dermatology disorders using herbal medications: summary. *International Journal of Indigenous Herbs and Drugs*, 1-14. <https://doi.org/10.46956/ijihd.v9i1.568>
- [42]. Guleria, P, Joshi, S, Parmar, S, Sharma, T, Chaudhary, A, Kumar, P, & Ashawat, M. S. (2025). Decoding acne vulgaris: Insights into pathogenesis, treatment modalities, diagnosis and recent advancements. *Recent Advances in Inflammation & Allergy Drug Discovery*, 19(1), 18-30. <https://doi.org/10.2174/0127722708312980240718093537>
- [43]. Jayronia, S, Mishra, S, & Kohli, K. (2024). The Essential Role of Herbal-based Therapies in Combatting Acne Vulgaris. *Letters in Drug Design & Discovery*, 21(17), 3694-3705. <https://doi.org/10.2174/0115701808328901240926153014>
- [44]. Thakur, M, Sobti, R, & Kaur, T. (2023). Medicinal and biological potential of Thuja occidentalis: A comprehensive review. *Asian Pacific Journal of Tropical Medicine*, 16(4), 148-161 https://journals.lww.com/aptm/fulltext/2023/16040/Medicinal_and_biological_potential_of_Thuja.2.aspx
- [45]. Hong, Y, Lin, S, Jiang, Y, & Ashraf, M. (2008). Variation in contents of total phenolics and flavonoids and antioxidant activities in the leaves of 11 Eriobotrya species. *Plant Foods for Human Nutrition*, 63(4), 200-204. <https://link.springer.com/article/10.1007/s11130-008-0088-6>
- [46]. Huang, J, Zaynab, M, Sharif, Y, Khan, J, Al-Yahyai, R., Sadder, M88 & Li, S. (2024). Tannins as antimicrobial agents: Understanding toxic effects on pathogens. *Toxicol*, 247, 107812. <https://doi.org/10.1016/j.toxicol.2024.107812> [Get rights and content](https://doi.org/10.1016/j.toxicol.2024.107812)
- [47]. Zámbořině Németh, É, & Thi Nguyen, H. (2020). Thujone, a widely debated volatile compound: What do we know about it?. *Phytochemistry reviews*, 19(2), 405-423. <https://link.springer.com/article/10.1007/s11101-020-09671-y>
- [48]. Srivastava, A, Jit, B. P, Dash, R, Srivastava, R, & Srivastava, S. (2023). Thuja occidentalis: an unexplored phytomedicine with therapeutic applications. *Combinatorial Chemistry & High Throughput Screening*, 26(1), 3-13. <https://doi.org/10.2174/1386207325666220308153732>
- [49]. Shubayr, N. (2023). Phytochemicals properties of herbal extracts for ultraviolet protection and skin health: A narrative review. *Journal of Radiation Research and Applied Sciences*, 16(4), 100729. <https://doi.org/10.1016/j.jrras.2023.100729> [Get rights and content](https://doi.org/10.1016/j.jrras.2023.100729)
- [50]. Verma, A, Zanoletti, A, Kareem, K. Y, Adelodun, B, Kumar, P, Ajibade, F. O & Dwivedi, A. (2024). Skin protection from solar ultraviolet radiation using natural compounds: a review. *Environmental Chemistry Letters*, 22(1), 273-295. <https://link.springer.com/article/10.1007/s10311-023-01649-4>
- [51]. Al-Harrasi, A, Bhatia, S, Behl, T, & Kaushik, D. (2022). Effects of essential oils on CNS. In *Role of Essential Oils in the Management of COVID-19* (pp. 269-297). CRC Press. <https://www.taylorfrancis.com/chapters/edit/10.1201/9781003175933-20/effects-essential-oils-cns>
- [52]. Soudry, Y, Lemogne, C, Malinvaud, D, Consoli, S. M., & Bonfils, P. (2011). Olfactory system and emotion: common substrates. *European annals of otorhinolaryngology, head and neck diseases*, 128(1), 18-23. <https://doi.org/10.1016/j.anorl.2010.09.007> [Get rights and content](https://doi.org/10.1016/j.anorl.2010.09.007)
- [53]. Tunon, M. J, Garcia-Mediavilla, M. V, Sanchez-Campos, S, & González-Gallego, J. (2009). Potential of flavonoids as anti-inflammatory agents: modulation of pro-inflammatory gene expression and signal transduction pathways. *Current drug metabolism*, 10(3), 256-271. <https://doi.org/10.2174/13892000978784636>
- [54]. Srivastava, A, Jit, B. P, Dash, R, Srivastava, R, & Srivastava, S. (2023). Thuja occidentalis: an unexplored phytomedicine with therapeutic applications. *Combinatorial Chemistry & High Throughput Screening*, 26(1), 3-13. <https://doi.org/10.2174/1386207325666220308153732>



- [55]. Singh, S, & Singh, T. G. (2024). Unlocking the mechanistic potential of Thuja occidentalis for managing diabetic neuropathy and nephropathy. *Journal of Traditional and Complementary Medicine*, 14(6), 581. [10.1016/j.jtcme.2024.04.009](https://doi.org/10.1016/j.jtcme.2024.04.009)
- [56]. Liu, H. M, Cheng, M. Y, Xun, M. H, Zhao, Z. W, Zhang, Y, Tang, W& Wang, W. (2023). Possible mechanisms of oxidative stress-induced skin cellular senescence, inflammation, and cancer and the therapeutic potential of plant polyphenols. *International Journal of Molecular Sciences*, 24(4), 3755. <https://doi.org/10.3390/ijms24043755>
- [57]. Hoque, M. B, Tanjila, M. J, Hosen, M. I, Hannan, M. A., Haque, P, Rahman, M. M., & Hasan, T. (2025). A comprehensive review of the health effects, origins, uses, and safety of tannins. *Plant and Soil*, 507(1), 221-240. <https://link.springer.com/article/10.1007/s11104-024-06768-7>
- [58]. Khan, M. T. (2004). *Phytochemical and biological studies of thuja occidentalis and its clinical evaluation in the treatment of verruca pedis*. University of London, University College London (United Kingdom).
- [59]. Kumari, S, Goyal, A, Sönmez Gürer, E, Algin Yapar, E, Garg, M, Sood, M, & Sindhu, R. K. (2022). Bioactive loaded novel nano-formulations for targeted drug delivery and their therapeutic potential. *Pharmaceutics*, 14(5), 1091. <https://doi.org/10.3390/pharmaceutics14051091>
- [60]. Khan, M. S, Aslam, M. M, Khan, N, Rehman, M, & Akhtar, N. (2025). Emerging Trends in Herbal Nanotechnology. *Herbal Pharmacopeia*, 188-212. <https://www.taylorfrancis.com/chapters/edit/10.1201/9781003544418-9/emerging-trends-herbal-nanotechnology>
- [61]. García-Hernández, L, Arenas-Islas, D, Ramírez-Ortega, P. A., Flores-Guerrero, M. U, & Neri-Enriquez, D. (2016). Green Synthesis, Characterization and Stabilization of Nanoparticles Silver with Thuja Orientalis Extract. *J Nanomater Mol Nanotechnol* 5: 6. of, 5, 6-8. 10.4172/2324-8777.1000198
- [62]. Yerezhpova, N, Kurmanbayeva, M, Terletskeya, N, Zhumagul, M, Kebert, M, Raşeta, M & Razhanov, M. (2024). New data on phytochemical and morphophysiological characteristics of Platycladus orientalis L. Franco and Thuja occidentalis L. conifer trees in polluted urban areas of Kazakhstan. *Forests*, 15(5), 790.

