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Yellow Miracle in Burns Treatment: *Hypericum perforatum*

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ABSTRACT

The skin is the body's largest sensory organ that covers the entire body. It plays crucial roles, such as regulating body temperature, maintaining fluid-electrolyte balance, providing a hemostatic balance, and protecting individuals from the harmful effects of external factors such as ultraviolet rays. Burns can occur due to exposure of body tissues to various traumas, including chemical, physical, electrical, and radiation. In determining the severity of a burn, it's crucial to consider various factors such as the patient's sociodemographic characteristics, location, depth, width, and any damage to vital organs. *Hypericum perforatum*, also known as St. John's Wort, has been clinically proven to be a safe and effective treatment option. It has a range of medicaluses, including wound and burn treatment, as well as properties that make it helpfulin treating depression, tumors, viruses, bacteria, inflammation, and pain. It's believedto have additional benefits, such as protecting the liver and aiding people with mentaldistress, mild depression, diabetes, obesity, and colds. St. John's Wort contains various antiviral, antioxidant, and anti-inflammatory substances. Research suggests that applying its extracts to a burn area can increase collagen production, halt the spread of infection, eliminate accumulated fluids, speed up the healing process, and promote healthy skin growth. This review aims to explore the potential effects of using the St. John's Wort plant for treating burns.

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INTRODUCTION

Skin is the largest sensory organ that covers the entire body. It regulates body temperature by providing a thermoregulator effect, maintaining fluid-electrolyte balance, and protecting individuals from external effects from ultraviolet rays (1). Burn is a word meaning; It occurs due to exposure of body tissues such as chemical, physical, electrical, and radiation to various traumas (2-5).

In the United States, approximately 338,000 people in 2016 and 460,000 people in 2017 received medical attention for burns, of which 40,000 were hospitalized (3-5). In Turkey, approximately 1 million people go to the hospital with burn complaints yearly, and about 12.000 of these patients receive inpatient treatment (6,7).

For burns to heal correctly, inflammation, granulation tissue formation (proliferation), and remodeling must be completed (8). After the burn occurs, with the passage of fluid into the extracellular space, there is an enlargement of the vessel diameter, and capillary permeability increases. With this process, neutrophils and monocytes go to the affected area to initiate the inflammatory process. The damaged area is cleared of necrotic spots and toxic materials thanks to the cellular response (9). Later, it begins with the migration of keratinocytes from living skin appendages in the burn area and generally covers the entire area within 5-7 days, and the proliferative phase begins. The third step is the reconstruction phase. In thisstage, scar tissue (scar) forms in the burn area (10).

It is crucial to consider the patient's sociodemographic traits, where the burn occurred, the depth and width of the burn, and any damage to vital organs. The American Burn Association categorizes burns as minor, medium, or extensive based on their width and depth. Minor burns; If they are 15% or less in adults, they are classified as 2nd-degree burns, 10% or less in a child, 2nd-degree burns, and 2% or less in an adult or child, 3rd-degree burns. Moderate burns; 15-25% of adults are classified as 2nd-degree burns, 10-20% of children are classified as 2nd-degree, and 2-10% of adults or children are classified as 3rd-degree burns (6). Major burns; If it is more than 25% in adults, it is classified as 2nd-degree burns; if it is more than 20% in a child, it is classified as 2nd-degree burns; and if it is more than 10% in an adult or child, it is classified as 3rd-degree burns. Inhalation burns, electrical burns, burns accompanied by another trauma (head trauma, intra-abdominal injury, fractures,

etc.), burn injury during pregnancy, presence of co-morbidities that add additional risk to the burn (DM, steroid use, immunosuppression, etc.), eye, ear, face, hand, foot, large joint, and genital area burns (11,12).

While the "rule of nines" provides simple and moderate accuracy to assess the total body surface area involved in burn patients, the Lund and Browder chart should be used in children. The rule of nines; Burn severity is calculated by dividing the body into parts: head-neck 9%, arms 9%, left leg 18%, right leg 18%, trunk anterior 18%, compartment posterior 18%, genital area and anal region (perineum) 1% (13).

Classification of burns; It is done in two ways, depending on the depth and factor of the burn (14,15). The burn category, according to its deep, is divided into four degrees (16). Primary degree burns; superficial burns of the epidermis. Erythema and pain are present. No bullae or infection. Secondary burn; It is a burn in which the entire epidermis is affected, and a part of the dermis layer is damaged. There are vesicles and bullae. Third-degree burns; All layers of the skin are damaged. Wide-area scar tissue is present. Fourth-degree burns are deep burns that reach the bone with damage to the epidermis, dermis, hypodermis, muscles, tendons, and ligaments. Individuals may not feel pain because of nerve damage (11,16). Classification according to the burn factor consists of thermal burns after scalding and flame (16), electrical burns (17), chemical burns (18), and radiation burns (19).

The burn patient must evaluate respiration, ensuring airway patency and circulation evaluation. If the patient needs it, treatment should be planned by the "ABCDE" algorithm in the principles of Advanced Trauma Life Support (Advanced Trauma Life Support). It is crucial to close the burn area with early and appropriate excision in patients who need emergency surgery. Cellulitis, impetigo, invasive infection signs, and symptoms that may develop due to deterioration of skin integrity in burn patients should be observed and detected in the early period. Effective burn dressings should be planned and implemented as soon as possible, using treatments like silver sulfadiazine or nitrofurazone to combat bacteria and suppress DNA/RNA synthesis and carbohydrate metabolism (7,20-23).

St. John's Wort

Humankind has sought the cure for diseases in nature since its existence (24-26). St. John's Wort plant, widely used since ancient times, is now commonly used in Turkey and worldwide.Saint John's wort (SJW), scientifically known as Hypericum perforatum, belongs to the Hypericaceae family. This family has over 1000 species and 55 genera, and SJW is classified under the Hypericum genus (27,28). See Table 1 for its taxonomic hierarchy.

Over 450 species in the Hypericum genus grow in tropical and subtropical regions across the globe, including Europe, Western Asia, North Africa, Madeira, and the Azores. They are primarily found in North America and Australia (29). *Hypericum perforatum* is a versatile plant that can thrive in various ecosystems, including pastures, bushes, forest clearings, and meadows (28). It can reach a height of 100-110 cm from the ground and is a perennial herbaceous plant with hairless mature stems and branches, as noted by Klemow in 2011 (29).

The plant's leaves are typically elliptical, oblong, or oval, measuring 1 to 3 cm in length and 0.3-1.0 cm in width, with smooth edges (30,31). When exposed to light, the leaves have translucent spots (32,33). The flowers are usually symmetrical, flat, or in clusters and hermaphroditic. The plant's fruit is an oval capsule; its seeds are numerous, brown, and approximately 1 mm long (29).

Table 1. Taxonomic hierarchy of *Hypericum perforatum.*

Kingdom	**Plantae – plantes, Planta, Vegetal, plants**
Subkingdom	Viridiplantae – green plants
Infrakingdom	Streptophyta – land plants
Superdivision	Embryophyta
Division	Tracheophyta – vascular plants, tracheophytes
Subdivision	Spermatophytina – spermatophytes, seed plants, phanérogames
Class	Magnoliopsida
Superorder	Rosanae
Order	Malpighiales
Family	Hypericaceae
Genus	Hypericum L. – St. Johnswort
Species	*Hypericum perforatum* L. – St. John's wort, common St. John's wort, Klamathweed, Klamath weed, St. Johnswort, common St. Johnswort

(https://www.itis.gov/servlet/SingleRpt/SingleRpt?search_topic=TSN&search_value=21454#null 18.04.2023).

Numerous studies indicate that *Hypericum perforatum* possesses bioactive components such as naphthodianthrones-anthraquinone, phloroglucinols, flavonol glycosides, biflavones, phenylpropanoids, proanthocyanidins, tannins, and xanthones (32-35). Additionally, it contains essential oils, fatty acids, and vitamins that exhibit bioactive properties as well. Table 2 provides a detailed summary of these components and their activities.

The usage areas of St. John's Wort plant, which has been popularly used in recent years; wound, burn treatment, antidepressant (46-48), antitumor (49), antiviral (50), antibacterial (51), antioxidant (52), anti-inflammatory (53), analgesic (54), hepatoprotective (55), mental distress, mild depression, diabetes, obesity, colds, fatigue (56). *Hypericum perforatum* has been studied in clinical trials and found to be effective and safe for therapeutic use.

Table 2. Bioactive components of Hypericum perforatum and their bioactivities.

Bioactive Natural Components	Compound	Bioactivite	Reference
Naphthodianthrones-anthraquinone	hypericin, pseudohypericin, and isohypericin; protohypericin, and pro-topseudohypericin (biosynthetic precursors of hypericin and pseudohy-pericin, respectively) cyclopseudohypericin, hypericin pseudohypericin	antiviral, photosensitizing, anticancer	(36)
Phloroglucinols	hyperforin, adhyperforin, hydroperoxycadiforin	antidepressant, antibacterial, cytotoxic, antiangiogenic, antidepressant, antiphlogistic	(37-39)
Flavonol glycosides	kaempferol, quercetin, luteolin hyperoside, soquercitrin, quercitrin, rutin, bi ¯avonoids including biapigenin and biapigenin	antifungal, MAO inhibit, offensive activity	(40)
Biflavones	3', 8"-biapigenin, amentoflavon, 6', 8"-diquersetin, catechins	antidepressant, antiphlogistic	(41)
Phenylpropanes	pcoumaric, chlorogenic, caffeic, vanillic, p-hydroxybenzoic, and ferulic acids	antioxidant, antiinflammatory, antimicrobial, antiallergic, hepatoprotective, and anticarcinogenic activities	(37,42,43)
Proanthocyanidins and tannins	Dimeric procyanidin b2, dimeric, trimeric, and tetrameric procyanidins	antiphlogistic, antioxidant, antiviral, antifungal, antibacterial	(37,44)
Xanthones	kielkorin, noratiriyol, mangiferin, 1,3,6,7-tetrahidroksiksanton	antimalarial, antimicrobial, antitumor, anti-alzheimer's antiviral, diuretic, cardiotonic, mao inhibitor	(44)
Other components	palmitic, isovalerianic, myristic, stearic, nicotinic, citric, and malic, tryptophan, γ-aminobutyric acid, and melatonin, nicotinamide, vitamin C, sugars (glucose, fructose, saccharose, and lactose), fatty acids, bisanthraquinone, glycosides, and hydroperoxycadiforin, monoterpenes a-pinene p-pinene, limonene, b-caryophyllene, myrcene, geraniol, germacrene d, b-farnesene, humulene, and larger amounts of longchain alkanols, hydrocarbons, and alkanols such as undecane, n-undecane, n-nonane, n-tetradecanol, 2-methyloctane and -decane, 2-methyl-dodecane, C16 and C29 alkanes and C24, C26, and C28 alkanols, and 2-methylbutenol.	The essential oils are beneficial for promoting neurite outgrowth and providing neuroprotection. They are commonly used in vitro for their antimicrobial and enzyme-inhibitory properties.	(45)

CHARACTERISTICS OF MAJOR COMPONENTS

Hypericum perforatum contains two significant metabolites, hypericin, and hyperforin, that are highly valued in the pharmaceutical industry. Hypericin, a major component, is a natural chromophore found in small black glandular structures on flower petals, stamens, leaves, and stems due to its chemical structure (57).

Hypericin, a natural photosensitizing agent, is used in anticancer photodynamic therapy (PDT) and photodynamic diagnosis (PDD) (58). Additionally, studies have shown that hypericin can act as a fungicidal (59) , and bactericidal agent (60) , as well as an effective antiviral agent (61).

Hypericum perforatum plant contains hyperforin, a significant component in its leaves and flowers (62). Multiple studies suggest that hyperforin has many beneficial properties, including anti-inflammatory, antiangiogenic, anticarcinogenic, antiproliferative, proapoptotic, anti-invasive, and antimetastatic activities (63). However, hyperforin is unstable when exposed

to light and oxygen. Therefore, the plant needs to be dried appropriately (64).

St. John's Wort and Burn

Studies have shown that St. John's Wort plant can effectively treat burns due to its antiviral, antioxidant, and anti-inflammatory properties. It helps increase collagen production, prevent infection, reduce fluid buildup, and promote skin healing (65,66). Recent research on burn treatment has highlighted the frequent use of this plant.

In a study by Albert et al. in 2002 and Medina et al. in 2006, it was determined that hyperforin contained in *Hypericum perforatum* inhibited cyclooxygenase-1 and 5-lipoxygenase and showed anti-inflammatory properties in the burn area (65,66).

In a study conducted by Saddiqe et al. in 2010, it was found that *Hypericum perforatum* healed within 48 hours in first-degree burns, and keloid formation was not found in burns with increasing degrees. It accelerated the burn healing process (67).

In 2011, Öz conducted a study on rats to explore how St. John's Wort affected the epithelization of burn wounds in an experimental model. The study found that using an extract of *Hypericum perforatum* L., specifically with 3% olive oil, positively impacted the epithelization of 2nd-degree burn wounds (68).

In 2013, Cabbaroğlu experimented on rats to study the effects of St. John's Wort on contact-type burns. The sample group was divided into four groups. The first group was treated with silver sulfadiazine, the second group received saline solution treatment, the third group was treated with H. perforatum, and the fourth group received *Hypericum perforatum* treatment. The results showed that compared to silver sulfadiazine treatment, *Hypericum perforatum* treatment significantly reduced edema, collagen discoloration, vessel damage, hair root loss, and gl. It was also found to reduce sebaceous secretions and protect the total number of hair follicles, vessels, and the thickness of the epidermis (66).

In 2016, Severcan conducted a specialty thesis to explore whether topical and systemic applications could treat deep second-degree burns in rats. The study involved dividing the rats into five groups and creating burns by exposing their backs to 70 °C water for 12 seconds using a thermostat bottle with a 7 cm2 mouth opening. It was determined that systemic and topical use of *Hypericum perforatum* in rats treated with saline, olive oil, and *Hypericum perforatum* decreased inflammation compared to the control group. Its systemic use accelerated recovery compared to all other groups (69).

CONCLUSION

Throughout history, people have used various plantpreparations to treat burns. Ongoing research has focused on the benefits and risks of using these preparations. St. John's Wort has been found to have antiviral, antibacterial, antioxidant, and anti-inflammatory properties that effectively treat burns. However, it is essential to note that St. John's Wort oil contains potent chemicals that can be harmful if misused. It should only be used under the guidance of a healthcare professional. Health team members can attend training sessions and conferences to learn more about St. John's Wort. Additionally, the public should be informed about the safe use of this plant. Despite its potential benefits, only a few academic studies have been conducted on St. John's Wort, and it is recommended that more research be done.

Conflicts of Interest

The authors declare no conflict of interest.

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