

## ***Developments in the Use of Natural Wound-Healing Drugs in Veterinary Medicine***

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### **Introduction**

#### ***Plants Used in Wound Healing in Animals***

With the advancement of technology, significant progress has been made in the pharmaceutical sector in treating diseases of different types. However, excessive use of medications has also led to issues such as the accumulation of unwanted substances in organs and similar problems. Today, despite all these various medications, the emergence of new diseases that cannot be treated has led scientists to search for more natural and additive-free treatment methods using extracts obtained from different parts of plants. This has resulted in the birth of phytotherapy. Recently, dietary supplements and various supportive products developed through phytotherapy have been commonly used for preventive purposes rather than treating diseases.

Phytotherapy is based on using herbal medicines to treat and prevent diseases in humans and animals. The practices of phytotherapy are quite ancient; the first written document related to phytotherapy can be found in the Nineve tablets belonging to the Sumerian, Akkadian, and Assyrian civilizations established in Mesopotamia around 3000 BC. It is known that these tablets mention the use of plant and animal-derived substances in the treatment of various diseases. During the Islamic civilization period, Ibn Sina and Al Gafini wrote significant works on herbal medicine (Calapai, 2015; Ferreira et al., 2014; Günergün & Etker, 2013).

Plant and herbal materials hold an important place within veterinary phytotherapy practices. Some bioactive chemical compounds synthesized by plants have medical

effects(Schlittenlacher et al., 2022; Tchetan et al., 2021; YİPEL et al., 2021). The medicinal properties of plants used in phytotherapy stem from the numerous active compounds within the plant kingdom. Often, these active substances extracted from plants are equivalent to synthetic drugs in terms of their therapeutic effects; therefore, they are primarily used in veterinary medicine as antibacterial, antifungal, antiparasitic, disinfectant, and immunostimulant agents (Severino et al., 2008; Yanar, 2022). Additionally, herbal medicines are also utilized to avoid potential side effects that may arise from the long-term use of synthetic drugs and to treat certain chronic diseases. As a result, Severino et al. (2008) state that phytotherapy is a beneficial support for traditional treatments in cases of severe illness(Severino et al., 2008). In veterinary medicine, plants have been used for various purposes throughout history. The plant *Urtica dioica* is used to stimulate egg-laying in chickens, *Scrophularia canina* is utilized for wound antisepsis in cattle, and *Sempervivum tectorum* is employed to accelerate digestion in calves. A study conducted on cows with endometritis reported that plants were more effective than antibiotics (Sharma et al., 2018). A study conducted on dogs with pyoderma, atopic dermatitis, otitis externa, wounds, and dermatophytosis reported the utilization of *Calendula officinalis* L. (Marigold), *Hypericum perforatum* L. (St. John's Wort), *Matricaria chamomilla* L. (syn. *Matricaria recutita* L., Chamomile) and *Salvia officinalis* L. yield positive results for their broad-spectrum antibacterial and antifungal effects(Tresch et al., 2019).

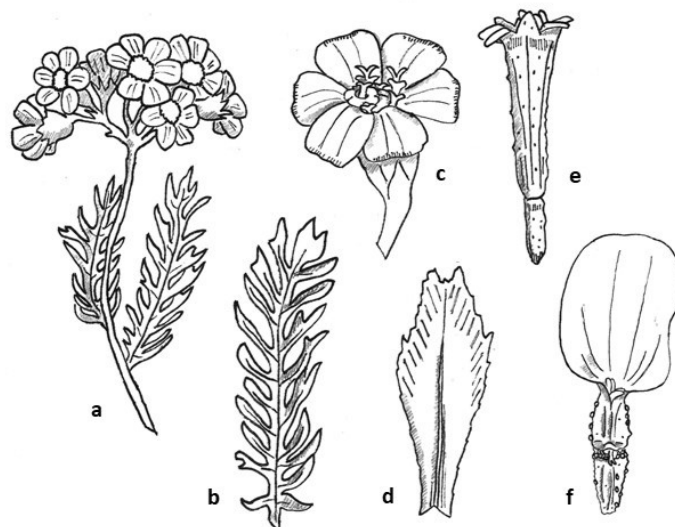
Wound healing in veterinary medicine often utilizes various plants, including **gotu kola**, **aloe vera**, **tea tree oil**, and **St. John's wort**. However, more clinical research is needed to establish the safety and efficacy of these herbal treatments (Gölgeli Bedir and Turgut, 2021). In this section, information will be given about the use of various plants in wound healing in animals:

#### *Achillea millefolium* (Yarrow)

*Achillea millefolium*, also known as “Sarisabır” (Yarrow), is a perennial flowering plant with wound-healing properties since ancient times; and has been used for medicinal purposes because of its anti-inflammatory, antimicrobial, and hemostatic effects (Figure 1)

#### Figure 1

Botanical line drawings of *Achillea moschata* Wulfen: (a) Plant in toto. (b) Bipinnate leaf. (c) Flower head. (d) Involucral bract (e) disk floret (f) ray floret. Original drawings by L. Colombo.(Bottoni et al., 2022).



Yarrow includes crucial phytochemical compounds like flavonoids (quercetin, luteolin, etc.) that have antioxidant properties and help reduce oxidative stress. These compounds prevent tissue damage by fighting free radicals and promote cell regeneration (Akbar, 2020). Another compound, sesquiterpenes, has antimicrobial and anti-inflammatory properties that reduce the risk of infection and speed up wound healing. Sesquiterpenes also reduce inflammation in the skin, allowing tissues to repair more quickly (Geana et al., 2023). Volatile oils such as 1,8-cineole and  $\alpha$ -pinene help prevent wound infections and regenerate tissue. As can be seen, the rich content of yarrow supports its ability to be a powerful wound healer (Tadić et al., 2017).

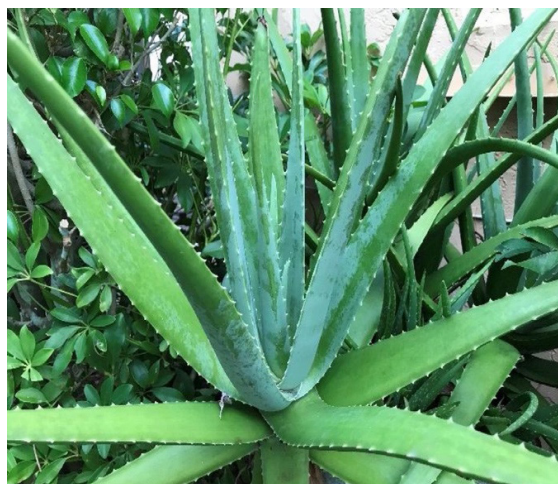
In the literature, *Achillea millefolium* has been supported by its wound-healing effect. In ancient times, soldiers used the plant to treat wounds and stop bleeding. It has been confirmed that the plant's anti-inflammatory and antimicrobial properties support this effect (Grigore et al., 2020). The control of inflammation is a critical factor in wound healing. Yarrow suppresses increased inflammation and allows tissues to heal faster (Ngo et al., 2020). The environment surrounding the wound is kept clean and sterile to facilitate optimal wound healing. Yarrow also contributes to the acceleration of wound healing by reducing the risk of infection of its antimicrobial properties. Studies have shown that the plant's antibacterial and antifungal properties are particularly effective in preventing infections (Zakeri et al., 2020). While the popularity of herbal treatments is increasing, yarrow is used in alternative medicine for wound treatment in animals (Jarić et al., 2018). The plant, which can be used as a natural support for skin injuries, cuts, and post-operative healing, has properties that prevent wounds from getting infected and reduce inflammation (Frański & Beszterda-Buszcza, 2023; Villalva et al., 2023). Yarrow is usually applied topically to wounds as an infusion or tincture. It has been observed that inflammation and infection are reduced on the wound surface where the plant is practical. It has been observed that wound healing time is reduced and inflammation is controlled in animals (cats and dogs) to which yarrow is applied (Ercil, 2017; Tresch et al., 2019; Uyar, 2017).

*Aloe vera* (L.) Burm (Syn: *Aloe barbadensis* Miller)

*Aloe vera*; belongs to the Asphodelaceae (Liliaceae) family and is a shrubby or tree-like, perennial, succulent, and pea-green colored plant (Figure 2) (Surjushe et al., 2008). *A. vera* has been the focus of extensive scientific research regarding its wound-healing properties.

### Figure 2

Aerial parts of *A. vera* (Kumar et al., 2019)



Several studies indicate that it may facilitate the wound-healing process through many different mechanisms. *Aloe vera* has been shown to reduce inflammation; and stimulate fibroblast proliferation, collagen synthesis, wound contraction, re-epithelialization, and angiogenesis. Furthermore, it has been shown to stimulate the production of growth factors, including transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1) and vascular endothelial growth factor (VEGF), at the wound site (Kaewrsisung et al., 2021). Additionally, it has been documented to have antimicrobial properties that facilitate these mechanisms (Jawad, 2014). Furthermore, aloe vera has been shown to accelerate wound healing by increasing collagen synthesis, influencing fibroplasia, and reducing wound size (Razi et al., 2021; Tariq et al., 2021). AL-Dhamary et al. (2024) reported that treatment with *A. vera* gel may result in faster wound healing compared to routine treatments (AL-Dhamary et al., 2024). Findings of studies conducted by Sutrisno (2024), Mara (2022), and Ali (2023) have shown that it has been used in multiple forms including gel, extract, and cream to accelerate the healing process of wounds (B. G. Ali et al., 2023; Dilla Sastri Mara, 2022; Sutrisno et al., 2024). The gel form has been associated with improved outcomes in terms of epithelialization rate and burn wound healing compared to conventional treatments such as silver sulfadiazine cream (Mohamad-Abadi et al., 2023). All studies support that it has the potential to serve as a natural and effective treatment to promote wound healing through its anti-inflammatory, antimicrobial, and collagen-stimulating effects.

*Aloe vera* has been recognized for its therapeutic activity in veterinary medicine because of its antimicrobial effects, making it an effective topical agent for managing wounds in animals (Jawad, 2014). Moreover, studies have shown that its secondary metabolites can promote wound-healing effects in various animal models, highlighting its potential for use in the veterinary field (Kusmardi et al., 2019). Hydrogel has been shown to increase the number of fibroblasts in socket wounds after tooth extraction in animals, confirming its positive effect on wound healing (Silvi Tiara Dewi & Susanto, 2021). Moreover, studies have shown that fresh and commercial gel can exhibit anti-inflammatory effects by reducing inflammatory mediators such as IL-6, thereby facilitating wound healing in animals (Mohamad-Abadi et al., 2023). The combined application of gel and microcurrent has been suggested as an effective treatment for open wounds in animals, highlighting the potential benefits of this approach in wound healing (Mendonça et al., 2009).

A study conducted by Drudi et al. (2018) evaluated the efficacy of this plant and silver sulfadiazine creams in promoting secondary wound healing in dogs and cats (Drudi et al., 2018). *Aloe vera* is renowned for its anti-inflammatory and antimicrobial properties, attributed to its bioactive compounds, including polysaccharides and vitamins. The study showed that *A. vera* facilitates the processes of epithelialization, collagen synthesis, and granulation tissue formation, thereby promoting a faster wound healing process. Furthermore, it has been shown to reduce inflammation and maintain a moist wound environment, thereby facilitating the healing process (Drudi et al., 2018). Traditionally used to prevent infections, the antimicrobial effects of silver sulfadiazine were found to be less effective in promoting wound healing, particularly in the epithelialization and scar formation processes, compared to *Aloe vera*. The trial showed that there was a statistically significant reduction in the size of wounds treated with *Aloe vera* and that it provided a more effective healing process. This effect is said to be related to the capacity of *A. vera* to increase localized blood flow and stimulate fibroblast and keratinocyte proliferation, which are crucial for tissue repair (Drudi et al., 2018). When Atiba et al. (2014) evaluated the healing efficacy of *Aloe vera* and silver sulfadiazine in the treatment of deep second-degree burns in dogs, they showed that *A. vera* was highly effective in promoting accelerated healing, particularly in terms of epithelialization and reduction of inflammation. Besides, its treatment in dogs was found to result in faster wound closure and superior quality tissue repair compared to silver sulfadiazine treatment (Atiba et al., 2014).

Another study examined the effects of topical *Aloe vera*, honey, and the combination



of both on wound healing in goats, resulting in the lowest bacterial counts, followed by *Aloe vera* treatment and combination treatment. Histopathological examination revealed that *A. vera* provided rapid tissue repair, complete wound contraction, and complete epithelialization compared to the other groups. Therefore, it can be concluded that *Aloe vera* L. alone is the most effective in promoting wound healing, followed by the combination of honey and honey alone (Roy et al., 2022).

Research on *A. vera* in veterinary medicine demonstrates its potential for therapeutic applications in promoting wound healing, reducing inflammation, and improving animals' health. Most studies support using *A. vera* as a valuable natural remedy in veterinary practice.

### *Calendula officinalis* L. (Marigold)

*Calendula officinalis*, a member of the Asteraceae family, is one of the economically important ornamental plants grown worldwide (Figure 3). It blooms in yellow, red, orange, and brown. *C. officinalis* L., commonly known as marigold, has long been recognized for its medicinal properties, particularly in the field of wound healing (Verma et al., 2018). Native to Central and Southern Europe, Western Asia, and the United States, this plant has been a cornerstone of traditional medicine for centuries. Recent scientific studies have further confirmed its therapeutic potential, making it a major topic of interest in contemporary medical research (Ashwlayan et al., 2018).

### Figure 3

*Calendula officinalis*. (Zhang et al., 2024).



In ethnoveterinary medicine, the use of medicinal plants such as *Calendula officinalis* for animal diseases is well documented. (Masika et al., 2000). Moreover, studies on herbal medicines from various regions such as Yemen have revealed the potential of plants such as *C.officinalis* and significantly succeeded in wound healing for animals (Alasbahi & Groot, 2020) ; Preethi & Kuttan, 2009). Flower extracts have strong anti-inflammatory, antimicrobial, and regenerative properties (Baghdadi et al., 2020; Patil et al., 2022), making them an excellent choice for treating wounds and skin conditions in animals (Chroho et al., 2021; Parente et al., 2012). These properties have made calendula-based treatments valuable for veterinary care and offer natural alternatives for healing.

The therapeutic effects of *Calendula officinalis* are due to its rich phytochemical content, including carotenoids, flavonoids, and triterpenoids, which contribute to its medicinal properties (Verma et al., 2018). These compounds are responsible for reducing inflammation and supporting tissue repair, because of their antioxidant effects. Topical applications of *C.officinalis* preparations have been found to enhance wound healing, accelerate re-epithelialization, and granulation tissue formation (Verma et al., 2018).

Flower extracts of the *Calendula officinalis* have stimulated tissue granulation in wounds. This process modulates and facilitates the expression of two important proteins, connective tissue growth factor (CTGF) and  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA), in the affected area (Shedoeva et al., 2019). In addition, it promotes wound healing by increasing the number of fibroblasts and collagen synthesis (de S Moraes et al., 2019; Dinda et al., 2015; Nowak-Terpiłowska et al., 2023). It has been reported that *C. officinalis* has a positive effect on angiogenesis, the formation of new blood vessels, which is crucial for tissue repair and wound healing (Dinda et al., 2016; Nahar & Choubey, 2024). This targeted treatment has proven effective in veterinary clinics for skin conditions such as surgical wounds, cuts, and ulcers.

Interestingly, using *C. officinalis* in combination with other herbal extracts has been shown to have even greater potential for wound care. Polyherbal formulations containing Calendula have been shown to accelerate the wound healing process by promoting fibroblast and keratinocyte proliferation and increasing angiogenesis at the injury site (Talekar et al., 2017). This synergistic interaction between different herbal extracts offers a natural and powerful approach to wound management, highlighting the effectiveness of such treatments for animals. Da Silva Ferreira et al. (2022) analyzed the phytotherapy compound's clinical and histological effects on surgical wounds in female dogs. This compound, containing *Calendula officinalis*, *Aloe vera*, *Symphytum officinale*, *Vitis vinifera*, D-Panthenol, and Denatonium Benzoate®, has shown promising results in veterinary postsurgical care. Reduced inflammation, rapid wound healing, and improved appearance of wounds were noted in treated dogs (da Silva Ferreira et al., 2022).

In another study, it has been found that a 2% non-ionic *Calendula officinalis* cream was used to treat a significant laceration wound in a young Quarter Horse, facilitating the healing process (Boscarato et al., 2020). This result is consistent with the broader scientific literature suggesting that Calendula extracts have anti-inflammatory and wound-healing properties that may be useful in treating equine wounds. It has been used to treat hoof-related wounds and infections in animals (cattle, goats, sheep, and pigs) (Walkenhorst et al., 2019). It has been reported that calendula-based creams and ointments are frequently used to treat external wounds, especially on animal hooves. This effect is due to the plant's active secondary metabolites, including triterpenoids and flavonoids, which facilitate tissue regeneration and reduce inflammation. The presence of antimicrobial properties of *C. officinalis* L. during wound healing also helps reduce the risk of infection and dependence on synthetic antibiotics, which is crucial in combating antimicrobial resistance (Walkenhorst et al., 2019).

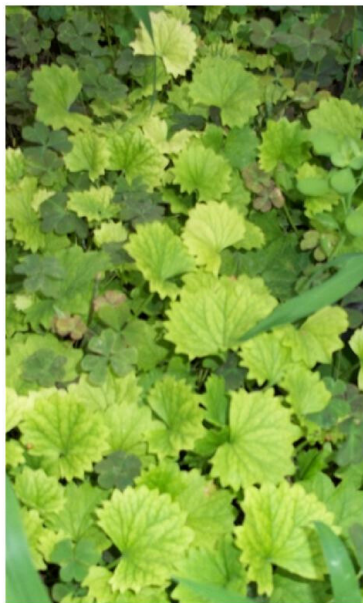
As a result, this plant has been identified as a valuable natural medicine in veterinary wound care, characterized by its capacity to stimulate fibroblast proliferation, promote angiogenesis, reduce inflammation, and accelerate healing. Calendula's long history in traditional medicine, supported by modern scientific evidence, positions it as a promising herbal alternative for treating animals.

### *Centella asiatica* (Gotu Kola)

*Centella asiatica* (Gotu kola), is a thin-stemmed, green-colored, leafy plant that grows in many temperate and tropical swamps in the world (Figure 4). It is a medicinal plant known in traditional medicine for its wound-healing, anti-inflammatory, and antioxidant properties. This plant, which is widely used in Southeast Asia, is also frequently used in wound treatment, skin regeneration, and anti-inflammatory treatments in modern medicine (Orhan, 2012).

**Figure 4**

*Centella asiatica* (L.) Urban (Apiaceae) (Orhan, 2012).



The wound-healing properties of *Centella asiatica* are due to its triterpenoids (asiatic acid, madecassic acid and asiaticoside). These components increase collagen production by promoting fibroblast proliferation and accelerate tissue repair. It has been stated that *Centella asiatica* accelerates the wound-healing process with its asiaticoside content and exhibits healing effects at the cellular level. Animal studies have reported that *Centella Asiatica* extract significantly increases wound closure and epithelialization processes (Shukla et al., 1999).

*C. asiatica* has an anti-inflammatory effect during the wound healing process. Triterpenoid components suppress inflammatory response by regulating macrophage and fibroblast activity. It has been observed that the triterpene components of the plant play an important role in suppressing inflammation and accelerating wound-healing (James & Dubery, 2009). Additionally, this mechanism reduces discomfort and inflammation, facilitating the healing of damaged tissue.

In addition, *Centella asiatica* contains powerful antioxidants that reduce oxidative stress. Components such as asiatic acid and madecassic acid neutralize free radicals and prevent cellular damage during the wound-healing. It has been stated that antioxidant compounds increase collagen synthesis, renew skin tissue, and help scars become less visible (Bonté et al., 1995). The synthesis of collagen represents a crucial stage in the wound healing process. The plant *Centella asiatica* has been demonstrated to facilitate the strengthening of injured tissue by accelerating this process. Studies have shown that *Centella asiatica* increases collagen production on fibroblasts and helps wound tissue repair more rapidly. This effect is thought to be especially important in reducing scar tissue (Maquart et al., 1990).

Veterinarians use this valuable plant for skin conditions such as burns, psoriasis, and eczema besides wound-healing treatment in clinics for dogs and cats. Triterpenoid components play an important role in their mechanisms. The use of the plant is increasing especially in reducing scars after surgery (Brinkhaus et al., 2000).

Controlling inflammation after injuries and surgical operations in animals is crucial for accelerating healing. *C. asiatica* is used especially in clinical applications in cats and dogs, especially after surgical interventions or traumatic injuries. For example, it is applied in the form of herbal ointment or topical cream for faster healing of stitches after surgical intervention, minimizing scars, and reducing inflammation and swelling



around the wound (Ro et al., 2021). *C. asiatica* has been shown to regulate inflammatory responses, thereby relieving localized edema and pain in the wound area. James and Dubery (2009) emphasized the effects of *Centella asiatica* in reducing inflammation and stated that triterpenoid compounds accelerate cellular repair by suppressing inflammation (James & Dubery, 2009).

Controlling inflammation after injuries and surgical interventions in commercially valuable horses is becoming a critical part of the healing process, because of *Centella asiatica*'s triterpenoids. Wounds can become infected and the healing process can be slowed down and prolonged due to horse mobility. Topical use of *Centella asiatica* on wounds can reduce these risks and accelerate the wound closure process (Girma et al., 2024).

*C. asiatica* has gained an important place in both traditional and modern veterinary medicine with its wound-healing potential. Scientific research strongly supports its contributions to wound-healing processes in animals. Also, its use in burns, scars, and tissue regeneration is becoming increasingly widespread in clinical applications.

#### *Hypericum perforatum* L.

It is a perennial herbaceous plant with a 30-80 cm height blooms bright yellow flowers between May and September (Figure 5).

*H. perforatum* (St. John's wort), is known for its wound-healing properties attributed to its various bioactive components such as naphthodianthrone, flavonoids, and phloroglucinols. These compounds have been shown to exhibit several pharmacological activities that contribute to the wound healing process, including anti-inflammatory, antimicrobial, and antioxidant effects (M. Ali et al., 2018; Seyhan, 2020; Yadollah-Damavandi et al., 2015). Several key areas are categorized to promote wound healing, such as improving cellular processes, modulating inflammation, and antimicrobial action for mechanisms belonging to *Hypericum perforatum*.

#### Figure 5

*Hypericum perforatum* (St. John's wort) (Suryawanshi et al., 2024)



*Hypericum perforatum* extracts have been shown to significantly facilitate fibroblast migration, a critical process for wound closure (Hostanska et al., 2012; Süntar et al., 2010). For example, Süntar et al. (2010) showed that the oily extract of *Hypericum*



*perforatum*, rich in hyperforin, promoted fibroblast migration without significantly affecting proliferation rates (Süntar et al., 2010). Additionally, Ali et al. (2018) reported that a niosomal topical drug delivery system containing *Hypericum perforatum* showed the potential to improve collagen synthesis in wound healing models (M. Ali et al., 2018).

*H. perforatum* is a plant used in traditional medicine for centuries to facilitate wound healing and treat injuries in animals. The anti-inflammatory and tissue repair properties have shown high efficacy in treating wounds and injuries. It has been one of the medicinal plants used as an alternative to allopathic drugs in organic agriculture, especially within certified organic programs. *Hypericum perforatum* is frequently used together with other plant species such as *Symphytum officinale* and *Calendula officinalis* for the treatment of various conditions, including abscesses and skin injuries (Lans et al., 2007).

In the study conducted by Ali et al. (2018), *Hypericum perforatum* extract, standardized for compounds such as hyperforin and hypericins, was applied with niosomal gel in treating of wounds in dogs. This gel; prepared using 80% ethanol extract and niosome technology, showed significant wound healing effects in an in vivo test in dogs. The reduced inflammation targeted for healing, accelerated proliferative rate, and complete wound' re-epithelialization within 21 days were achieved. In addition, these results were more effective than the results observed in the control and panthenol cream groups, indicating that *H. perforatum* has the potential to be used in transdermal wound treatments (M. Ali et al., 2018). Carnevali et al. (2019) evaluated the efficacy of a plant-based formulation containing neem oil and *Hypericum perforatum* extract in healing wound myiasis in domestic animals. Wounds caused by *Wohlfahrtia magnifica* larvae healed within 10 to 32 days without further infestation or bacterial complications and without using any antibiotics or disinfectants. The natural formulation was effective in treating wounds and promoting healing without toxic side effects and was presented as a safer alternative to creolin and insecticides (Carnevali et al., 2019).

The study conducted by Markovic et al. (2021) investigated the ethnopharmacological applications of medicinal plants in Pirot County, Eastern Serbia. In interviews with 631 local residents, a total of 192 plant species were frequently used, 46 of which were used in veterinary medicine. The most commonly used plants include *Cichorium intybus*, *Hypericum perforatum*, and *Rumex patientia*, primarily used to treat diarrhea, wounds, skin conditions, and fever in farm animals. The most commonly used plant families are *Asteraceae*, *Hypericaceae*, and *Polygonaceae*. The findings provide valuable insights for potential phytopharmacological studies in veterinary care (Marković et al., 2021).

### ***Melaleuca alternifolia* (Maiden & Betche) Cheel (Tea Tree)**

*Melaleuca alternifolia* oil (Tea Tree; Çay ağacı), is an essential oil known for its antimicrobial, antifungal, and anti-inflammatory properties. This oil has recently been applied clinically by veterinarians for various skin problems and wound treatments in cats and dogs. However, it should be used with caution due to toxicity.

Tea tree oil is an essential oil derived from the *M. alternifolia*, which is native to Australia and can grow up to 5-7 meters tall and is in the form of a shrub (Figure 6). Due to its strong antiseptic effect and wide range of use, it is exported. Fresh leaves and branch tips collected from plants during the flowering period are used to obtain essential oil (Sürme et al., 2020).

**Figure 6***Tea tree (Melaleuca leucadendra)* (Köhler, n.d.)

Tea tree oil has been used in traditional medicine for centuries in various forms, especially for antiseptic purposes (Gölgeli Bedir and Turgut, 2021). Tea Tree Oil has a broad-spectrum antimicrobial effect, especially in this way the terpinen-4-ol and  $\alpha$ -terpineol components it contains. Studies have shown that Tea Tree Oil is effective against bacteria such as *Staphylococci* and *Streptococci* and is used in skin infections in dogs (Fitzi et al., 2002). The positive effects of tea tree oil have been shown in frequently seen skin diseases such as pyoderma. It significantly reduces symptoms of pruritus, erythema, pustules, abscesses, crusting, irritation, alopecia, and skin thickening (Szewczuk et al., 2023). In an open, multicenter study of 53 dogs with chronic dermatitis and pruritus, when 10% tea tree oil cream was applied twice daily for 4 weeks, veterinarians observed a good or very good response in 82% of the dogs, a moderate response in 7.8%, and an inadequate response in 9.8%. At the end of the study, a strong and significant reduction in symptoms was observed (Fitzi et al., 2002). When a 10% tea tree cream was applied twice daily to a dog with localized pruritic dermatitis, 71% of the animals treated with tea tree oil cream had relief from pruritus and alopecia after 10 days (Reichling et al., 2004). The antifungal effect of this oil provides relief from redness and itching that occur on the skin in fungal infections. Veterinarians use it topically, especially in cases of dermatitis caused by fungi such as *Malassezia pachydermatis* and *Microsporum canis* (Tong et al., 1992). Another study reported that tea tree oil is also effective against fungal infections and has been used successfully against *Malassezia* and *Dermatophytes* species, especially those common in cats and dogs (Weseler et al., 2002). The anti-inflammatory properties of tea tree oil facilitate the alleviation of inflammatory reactions on the skin. The topical application of tea tree oil in the treatment of wounds has been demonstrated to reduce inflammation and contribute to the acceleration of skin tissue renewal (Koh et al., 2002). Tea Tree Oil, applied topically by veterinarians during the healing process after surgical procedures in cats and dogs, can help prevent wound infections and support rapid healing tissue (Fitzi et al., 2002).

Although Tea Tree Oil has strong antimicrobial and anti-inflammatory properties, it should be used carefully, especially in cats. This plant can cause toxicity in case of excessive exposure or incorrect use during use in animals (Khan et al., 2013). Using this

oil in high doses or undiluted in cats can cause neurological toxicity, ataxia, drooling, depression and, even coma. A study has shown that cats are sensitive to tea tree oil and that toxic effects can occur even at low doses (Bischoff & Guale, 1998; Elliott & Seawright, 1993). In another study conducted on cats, a topical application of 100% tea tree oil was performed on Ankara cats and the cats experienced hypothermia, decreased coordination, and tremors. The study determined that the cats' liver enzymes were elevated. The accumulated urine from the cats was positive for terpinen-4-ol, a component of tea tree oil. One cat was reported to have died in this study (Bischoff & Guale, 1998). In dogs, this oil is generally considered safe when used in a controlled manner. However, veterinarians recommend that the oil be diluted correctly and used only at certain concentrations. Typically, 1-2% diluted solutions are considered safe for topical applications (Helton & Werner, 2018). In a study, it was determined that the undesirable symptoms in dogs applied with pure tea tree oil were depression, lethargy, apathy, paresis, weakness, ataxia, tremors or muscle twitching, and rarely vomiting, coma, lying in a horizontal position, dermatitis, pruritus or rash, and elevated liver enzymes (Khan et al., 2013). Death occurred when 0.3-0.4 ml of tea tree oil was accidentally administered intravenously to an English shepherd dog. In another study conducted on dogs, 28.5 ml of pure tea tree oil was applied through the skin, and after the 3rd dose, the dog became ataxic and died (Khan et al., 2013). When 7 to 8 drops of tea tree oil were applied undiluted as a flea repellent, partial paralysis of the hind legs, ataxia, and depressive behavior were observed in dogs (Poppenga, 2007).

Tea tree oil is an effective natural treatment agent for dermatological problems, skin infections, and wound healing in cats and dogs. However, it should be used with caution in cats due to the risk of toxicity. Diluted forms are considered safe by veterinarians for topical application. Overdosage should be avoided and caution should be given to cat and dog relatives about the careful use of the oil.

### ***Symphytum officinale* L. (Comfrey)**

*Symphytum officinale* is a perennial flowering plant from the Boraginaceae family (Figure 7). It can bloom in blue, purple, pink or white. (Trifan et al., 2024) Comfrey (*S. officinale*) is traditionally recognized for its wound-healing properties, which are attributed to its anti-inflammatory, and analgesic effects and its capacity to stimulate tissue regeneration and promote wound healing (Le et al., 2021).

#### **Figure 7**

*Symphytum officinale* (Photo by Adriana Trifan) (Trifan et al., 2024)



The plant has a long history of therapeutic use, with records dating back to the 16th

century, particularly for improving wound healing (Gomes et al., 2010). Comfrey is renowned for its efficacy in treating various types of wounds, bone fractures, and bruises in traditional medicine (Bagheri et al., 2021). The root extract of the plant has been found to exhibit anti-inflammatory effects by influencing NF- $\kappa$ B signaling, which can help reduce inflammation in wounds, and is widely used for the management of musculoskeletal disorders, wound healing, and inflammatory conditions (Seigner et al., 2019). The wound-healing properties of comfrey (*Symphytum officinale*) have been recognized in the veterinary field. Several studies have shown that comfrey root preparations, known for their analgesic and anti-inflammatory properties, can facilitate wound healing in animals (Yang et al., 2011). The anti-inflammatory and analgesic effects of the plant, together with its ability to stimulate tissue regeneration, make it a valuable natural remedy for wound management in veterinary practice (Inkeniene Asta Marija & Vaiciuleviciene, 2023). Bioactive compounds found in comfrey, including allantoin, choline, and rosmarinic acid, are responsible for the anti-inflammatory and wound-healing effects observed in this plant (D'urso et al., 2020; Kučera et al., 2004). These compounds contribute to the plant's capacity to reduce inflammation and facilitate tissue repair (Kučera et al., 2004). Topical application of the plant's roots has been shown to reduce inflammation (Dähnhardt et al., 2020). In addition, comfrey has been used in folk medicine as an externally applied poultice to facilitate wound healing (Melnik et al., 2022). Its effectiveness in this regard is attributed to its capacity to accelerate superficial wound healing. The therapeutic properties of comfrey include anti-inflammatory, analgesic, granulation-promoting, and anti-exudative effects. Comfrey-based treatments such as herbal creams can offer a natural and effective approach to managing wounds and promoting healing in veterinary medicine.

### Other Herbs

Mathan Thailam is formulated using a blend of *Acalypha indica*, *Datura metel*, and Coconut oil besides copper sulfate, known for its wound-healing properties. The inclusion of copper sulphate in certain formulations is noteworthy because copper is a vital component in angiogenesis, collagen synthesis, and stabilization of extracellular matrix proteins. These processes are essential for effective wound healing (K et al., 2019). The anti-inflammatory properties of Mathan Thailam contribute to the reduction of swelling and pain observed at the wound site. This is especially advantageous for chronic wounds where inflammation can hinder healing. Moreover, the herbal components of Mathan Thailam have been shown to exhibit antimicrobial activity, which helps prevent infection, a common complication in wound healing (Selvaraju et al., 2022).

In a recent study, Selvaraju et al. (2022) demonstrated that Mathan Thailam was effective in addressing post-cesarean wound dehiscence in a Kangayam cow with uterine torsion (Selvaraju et al., 2022). After the surgical procedure, the cow exhibited a significant postoperative complication of reopening of the surgical wound and subsequent infection. Conventional methods used to re-seam the wound were unsuccessful due to the wideness of the opening. Mathan Thailam was applied topically for five days after regular wound cleaning. The wound was found to show significant healing with granulation tissue formation and after one month, the cow's wound was completely healed. Researchers have mentioned the potential of Mathan Thailam as an alternative treatment in veterinary care, especially for chronic or post-operative wounds, and have also highlighted its rejuvenating properties ((Selvaraju et al., 2022).

Although papain, an enzyme derived from papaya, is well documented in human medicine for its wound-healing properties, its applications in veterinary medicine have not yet been widely explored.

It has been investigated the effectiveness of natural remedies, including papain gel and sunflower oil, in treating severely necrotic wounds in dogs (Porsani et al., 2016). The study included three cases in which dogs with extensive necrotic wounds were treated with papain-gel accelerated healing by promoting tissue granulation, debridement of



necrotic tissue, and overall faster healing. In one case, sunflower oil, known for its anti-inflammatory and antimicrobial effects, was also used to support healing. In addition to being effective, these treatments are low-cost and accessible alternatives for wound management in animals (Porsani et al., 2016). Orlandini et al. (2017) described the use of papain cream and lyophilized parsley root extract (*Petroselinum crispum*) in the treatment of an abscess caused by a multiresistant *Escherichia coli* strain in a horse (Orlandini et al., 2017). Papain, a proteolytic enzyme, is renowned for its wound healing and anti-inflammatory properties, while parsley root extract is known for its antimicrobial activity. The combination of these two natural drugs was effective against the resistant bacterial strain when applied to the infected area of the horse. The treatment resulted in a significant reduction in infection and inflammation, thus demonstrating the potential of these alternative therapies in the management of difficult bacterial infections in veterinary medicine (Orlandini et al., 2017).

In conclusion, the resurgence of interest in phytotherapy serves to highlight the potential of plant-based treatments in veterinary medicine. As evidenced throughout history and corroborated by recent research, plants and their bioactive compounds represent a natural and effective alternative to synthetic drugs for managing various conditions, including wound healing. The utilization of plants such as *Calendula officinalis*, *Hypericum perforatum*, and *Aloe vera* highlights their potential as antibacterial, antifungal, and anti-inflammatory agents with minimal adverse effects. While traditional knowledge provides a robust foundation, modern scientific validation is imperative to optimize the utilization of phytotherapy in veterinary medicine. This includes conducting rigorous clinical trials to establish efficacy, standardize dosages, and ensure safety. Enlargement of our understanding of plant-based treatments will not only enhance their integration into veterinary practice but also provide sustainable and additive-free solutions to the growing challenges posed by drug resistance and synthetic medication side effects. There is a need to screen for new plants, many of which have especially antimicrobial, anti-inflammatory, analgesic, and antioxidant effects for wound treatment in the future. Consequently, the continued exploration of veterinary phytotherapy promises significant benefits for animal health and the broader ecological balance.

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