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To Formulate Film Forming Spray using Quercus Infectoria (Oak Gall) for Wound Healing Activity

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I'd like to thank The **ATMIYA UNIVERSITY** for providing us with the opportunity to work on the project (To formulate film forming spray containing Quercus infectoria gall extract for wound healing activity). Last but not least, I would like to express my gratitude to our other faculty members, family, siblings, and friends for their invaluable assistance, and I am deeply grateful to everyone whohas contributed to the successful completion of this project.

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ABSTRACT

Natural resource-derived compounds have been used in traditional medicine for as long as anybody can remember to influence the wound healing process. In compared to modern pharmaceuticals, these substances have a reduced toxicity potential and fewer side effects. An alcoholic extract of Q. infectoria galls was proven to be helpful in a variety of animal models of inflammation and wound healing.

Problems with conventional preparations include the likelihood of drug leftovers remaining after use in patch formulations, which enhances the chance that these remnants will be intentionally abused. Patch preparations are often linked to hypersensitivity, irritation, and blistering. When medications are difficult to stable and may crystallize during storage, there are typically issues with expanding output. Because they are administered with fingers, other semisolid formulations are more prone to cause wound cross-inflammation. These formulations are also more likely to adhere to clothes when the patient is moving.

The Spray Film Forming System (SFFS), which has the potential to be effective for a range of wound types, is at the leading edge of wound care technology. Such configurations are beneficial for prolonging the utility of active components, minimizing illness transmission, and promoting quick recovery. Whether the targeted effect is systemic or local, there are various advantages to employing a topical route for medication delivery. Avoiding first-pass metabolism, low pH and enzyme activity in the gastrointestinal system, and a large surface area are all examples. Improvements in therapeutic effectiveness. Because of their efficacy or pharmacokinetic profile, drugs applied to the skin often take the form of a patch, gel, lotion, cream, ointment, or spray.

As a result, the goal of this research is to create a film-forming spray that blends natural herbs or old and modern formulations for speedier wound healing. Based on multiple research and reports, ensure that the proper formulation is created by establishing the right concentrations of polymer system and solvent, as well as the right oak gall extraction ratio, to generate the right film-forming spray. Simply mixing film-forming polymers with an active extract of Oak gall (Quercus infectoria) yielded the spray solution. The result was a brilliant yellowish solution. Gall might be taken as a decoction, powder, or poultice, according to traditional sources. They were needed in a variety of situations. These findings support the traditional belief that Q. infectoria has the ability to heal wounds, suggesting that it would be an excellent herbal component to a film-forming spray for wound treatment. The findings of this study back up long-held assumptions regarding what promotes wound healing. The scientific results of the research also gave an explanation for its wound healing qualities.

The film forming spray created as a consequence of this endeavor has a skin-friendly pH and produces a film that is smooth, glossy, flexible, opaque, uniform, sticky, and peelable.

Keywords:- *Film Forming Spray, Oak Gall* ***(****Q. Infectoria****).***

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CHAPTER ONE
INTRODUCTION

A. Human Skin

The human skin is the organ that is most readily seen on the surface of the human body and is also one of the organs that is the most extensive and the most extensive. The surface of the body is responsible for both providing protection and responding to the sensory inputs that are brought in from the surrounding environment.

The skin has a surface area of around 2 square meters, weighs about 4.5 to 5 kg, and accounts for about 16% of the total body weight.

The skin is divided into three basic layers, which are as follows:

- The epidermis is a very thin layer that is located on the surface of epithelial tissues.
- Dermis: connective tissue that is denser and more superficial
- The hypodermis, also known as the subcutaneous layer, is located under the dermis but is not technically considered to be skin. This layer contains areolar and adipose tissue.

According to Bowler et al. (2001), a wound is any breach in the skin or mucosa membrane that makes it possible for bacteria and other pathogens to enter the body and cause an infection. The rich environment that is necessary for the proliferation of microorganisms is provided by wound tissue. It is marked by hypoxia, necrosis, and, in many instances, a decreased immunological response as a consequence of inadequate immune effector molecule delivery as a result of damaged blood arteries (Bowler et al., 1999). These characteristics may be seen in ischemic heart disease. (N. Darogha, 2009)

One of the most pressing issues in worldwide public health is the care of wounds. A considerable proportion of persons become incapacitated as a consequence of wounds. a cut or other wound with compromised tissue that has lost function as a result of trauma (physical, chemical, microbiological, immunological, or otherwise). For the purposes of the Wound Healing Society, a wound is "physical injuries that results in an opening (or break) of the skin that causes disturbance in the normal anatomy and function of the skin." (Rodríguez-Iturbe et al., 1979)

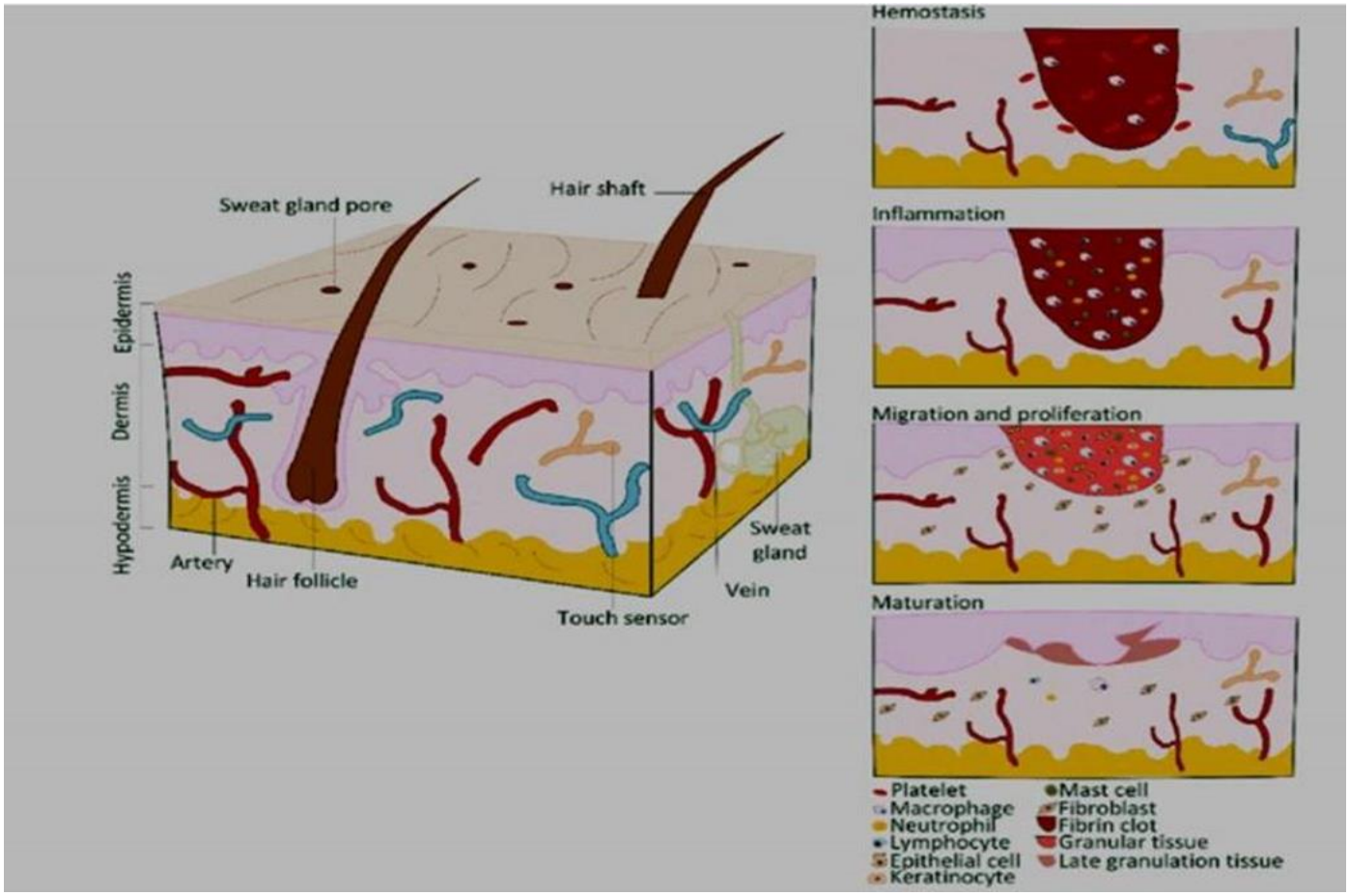

Fig 1 Skin Structure and Stages Wound Healing

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B. Pathology Of Wounds:

Wounds manifest as a consequence of any type of skin trauma that induces tearing or separation of the affected area. Proper wound healing is imperative for the restoration of anatomical continuity and functional integrity of the skin. A complex and intricate healing process is initiated in response to an injury; its purpose is to restore the integrity and functionality of the injured tissues. This procedure commences immediately following the injury. The lesion undergoes three distinct phases during the healing process: inflammation (0–3 days), cellular proliferation (3–12 days), and remodeling (3–6 months). These phases result from the ongoing interactions between cells and the matrix. Remodeling persists for 3–6 months, cellular proliferation for 3–12 days, and inflammation for 0–3 days. Multiple categories of tissues and cell lineages must collaborate in order for the body to recuperate correctly. Two of the processes involved are platelet aggregation and blood clotting, in addition to the formation of fibrin, an inflammatory response to the injury, changes in the composition of the ground substances, angiogenesis, and reepithelization. Collagen must successfully repair the disrupted surfaces before the healing process can be deemed finished. The essential concept behind efficient wound healing is to limit tissue damage while providing optimal tissue perfusion and oxygenation, correct feeding, and a moist wound healing environment in order to restore anatomical integrity and function to the affected area. This is accomplished by keeping the wound healing environment wet. The healing of a cutaneous wound is accompanied by an organized and recognizable series of biological events. This sequence starts with the closure of the wound and continues on to the repair and remodeling of wounded tissue. There have been significant advancements made in the pharmaceutical industry, but there is still a limited supply of medicines that can speed up the process of wound healing. Managing chronic wounds is a challenging problem, not only because of the high cost of treatment but also because of the possibility of unintended side effects. (*DESIGN AND CHARACTERIZATION OF TOPICAL ANTIBACTERIAL FORMULATION CONTAINING EXTRACT OF QUERCUS INFECTORIA GALLS | INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH*, 2023; *Ethnopharmacological Approaches to Wound Healing—Exploring Medicinal Plants of India - ScienceDirect*, n.d.; *Volume 14 (2023) | INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH*, n.d.)

Wounds may be categorized as follows based on their characteristics and severity:

- Wounds that are already closed, such as contusions, abrasions, and hematomas
- Open wounds: i.e., incised, lacerated, penetrating and crushed

Depending on the severity of the injury, a wound may be classified as one of the following:

- Simple wound: in this case, the damage is limited to the skin.
- Complex wound: a wound that affects the underlying tissues as well as tendons and other connective tissue.

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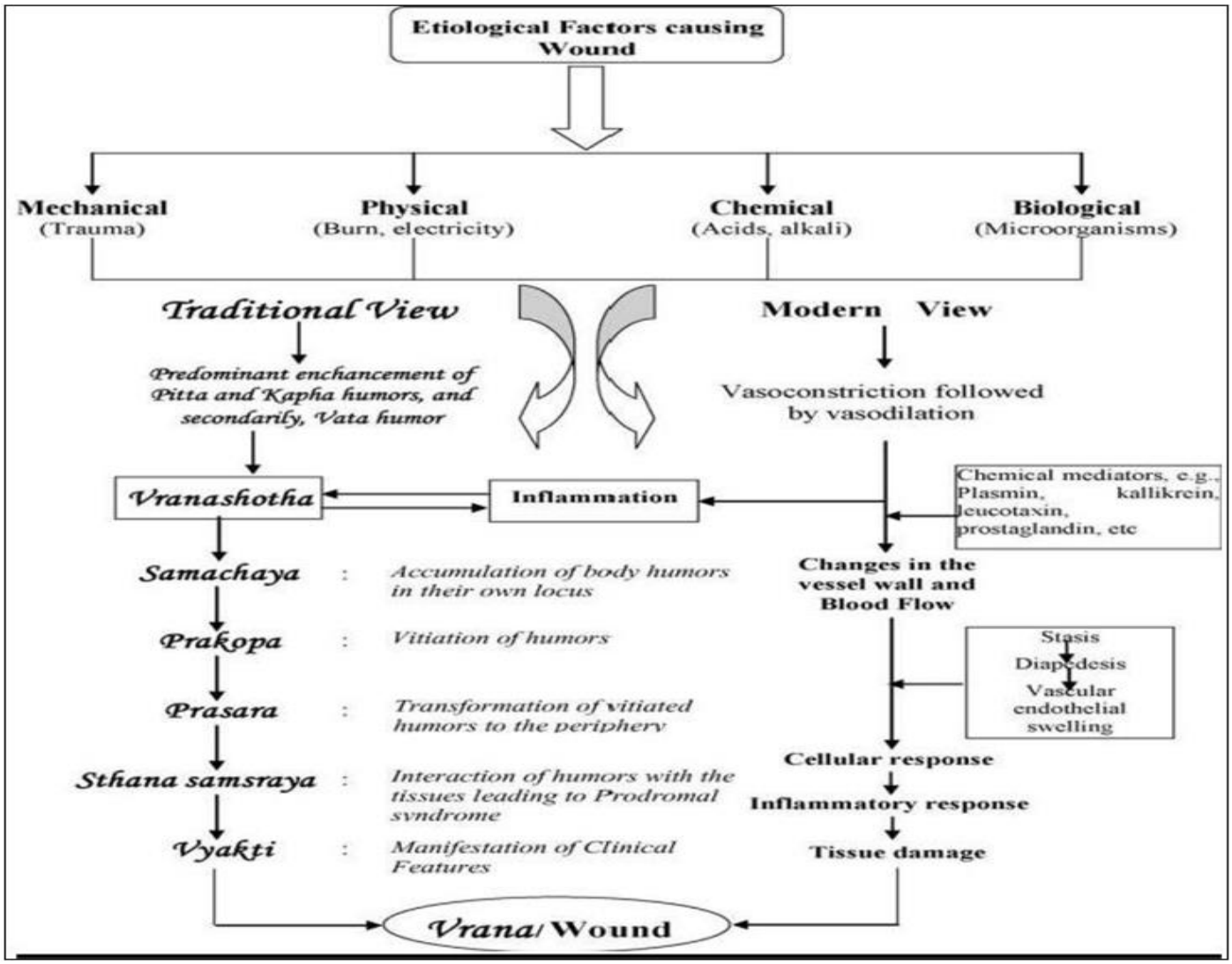

Fig 2 Comparative Representation of Pathogenesis of Wound Repair InAyurveda and Modern Days

➢ *Healing of Wound Can Occur By:*

- *Wound Healing Process*

Wound healing is a complex process that involves a series of overlapping stages. The type of wound healing depends on the extent of tissue damage and the presence of infection.

✓ *Primary Intention*

Primary intention healing occurs when the wound edges are clean and closely opposed, allowing for rapid closure. This process typically follows surgical incisions and minor cuts.

➢ *Stages of Primary Intention Healing*

- *Inflammation:*

The initial phase of healing involves inflammation, characterized by redness, swelling, heat, and pain. This inflammatory response serves several important functions:

✓ *Cleansing the Wound:*

White blood cells, particularly neutrophils and macrophages, migrate to the wound site and engulf cellular debris and bacteria, initiating the process of wound cleansing.

✓ *Initiating Angiogenesis:*

Inflammatory mediators, such as vascular endothelial growth factor (VEGF), stimulate the formation of new blood vessels, ensuring adequate oxygen and nutrient supply for the healing process.

✓ *Preparing the Wound Bed:*
Fibroblasts, the primary cells involved in wound healing, are activated by inflammatory mediators and begin to produce collagen fibers, providing structural support for the healing tissue.

- *Proliferation:*
The proliferation phase is characterized by the growth of new cells to bridge the gap between the wound edges.

✓ *Epithelialization:*
Epithelial cells from the edges of the wound migrate across the granulation tissue, covering the exposed surface and restoring the integrity of the epidermis.

✓ *Angiogenesis:*
Continued angiogenesis ensures a rich blood supply to support the growing tissue.

✓ *Fibroblast Activity:*
Fibroblasts continue to synthesize collagen fibers, strengthening the wound.

- *Maturation:*
The final stage of primary intention healing involves the remodeling and maturation of the scar tissue.

✓ *Collagen Remodeling:*
Collagen fibers are reorganized, increasing the tensile strength of the scar.

✓ *Vascularization:*
The density of blood vessels in the scar gradually decreases, giving the scar its characteristic pale appearance.

✓ *Scar Maturation:*
Over time, the scar becomes flattened and less noticeable.

➢ *Secondary Intention*
Secondary intention healing occurs when the wound edges are separated or there is significant tissue loss, preventing immediate closure. This type of healing is often associated with larger wounds, such as burns or deep cuts.

➢ *Stages of Secondary Intention Healing*

- *Inflammation:*
The inflammatory phase is similar to primary intention healing, involving cleansing, angiogenesis, and preparation of the wound bed.

- *Proliferation:*
Granulation tissue, a vascularized tissue composed of fibroblasts, macrophages, and new blood vessels, fills the wound cavity.

✓ *Angiogenesis:*
Granulation tissue is highly vascular, providing adequate blood supply for the healing process.

✓ *Fibroblast Activity:*
Fibroblasts within the granulation tissue continue to produce collagen fibers, gradually filling the wound with new tissue.

✓ *Epithelialization:*
Epithelial cells from the wound edges migrate over the granulation tissue, restoring the integrity of the epidermis.

- *Maturation:*
Maturation involves the remodeling and maturation of the scar tissue, similar to primary intention healing.(*Clark, R. A. (1996). Wound Healing: Overview and Principles. In The Molecular Biology of Wound Healing (Pp. 3-50). Springer, New York, NY.*, n.d.; *Landen, N. K., & Singer, A. J. (2013). Design and Evaluation of Cellulare and Tissue-Based Products for Wound Healing and Tissue Regeneration. In Principles of Regenerative Medicine (Pp. 249-268). Academic Press.*, n.d.; *Schultz, G. S., & Wysocki, A. (2009). Wound Healing. In The Journal of Clinical Investigation (Vol. 119, No. 8, Pp. 2191-2199). American Society for Clinical Investigation.*, n.d.; Takeo et al., 2015)

Herbal treatments are becoming more popular as people realize that they are not only effective but also much safer than conventional pharmaceuticals. It is envisaged that the use of plant extracts as an alternative to chemical drugs would lead to the production of promising outcomes in the treatment of a range of illnesses. Herbal remedies have been employed as both primary and secondary treatments in times of crisis ever since the beginning of recorded history. For instance, while cutting vegetables, ground turmeric is used. Turmeric acts as an antibacterial and anti-inflammatory agent, and it also has a number of uses in the medical field. In treatment throughout the course of many centuries, pulped juices or herb extracts derived from various plant components were often employed. The need for a powerful and practical herbal medicine is growing in today's society.(*DESIGN AND CHARACTERIZATION OF TOPICAL ANTIBACTERIAL FORMULATION CONTAINING EXTRACT OF QUERCUS INFECTORIA GALLS | INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH*, 2023; *Volume 14 (2023) | INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH*, n.d.)

The present study aimed to formulate film forming spray containing Quercus infectoria gall extract.

Quercus sp., which belongs to the family Fagaceae, is a kind of tree that can be found in forests all over the globe and may be found in a variety of geographic regions in the northern hemisphere. The appearance of the many species of plants belonging to the Quercus genus is distinct from one another in terms of their morphology. There are species of Quercus that may grow to be as tall as mountains, while others can be as little as shrubs or trees. In Iran, there are fifteen distinct species of Quercus, and traditional Iranian medicine has long made use of the trees for a variety of therapeutic reasons.(Mahboubi, 2020)

Since they are less toxic and have less side effects than conventional medications, chemicals derived from natural resources have been utilized in traditional medicine to control the wound healing process since ancient times.(Abu-Al-Basal, 2010) The World Health Organization (WHO) reports that over eighty percent of the world's population utilizes alternative treatments based on plant-based therapies for skin-related disorders, including wounds. (Anupama, 2016) The genus Quercus (Fagaceae), one of the plants utilized for this purpose, has 23 species in Turkey's flora, four of which are indigenous (Hedge & Lamond, 1982). In the practice of traditional medicine, the use of a decoction made from Quercus species is regarded to be an effective pharmacological agent for treating wounds and burns(Kaur et al., 2004). Significant pharmacological features of this plant, such as anti-inflammatory(Kaur et al., 2004), antibacterial, antioxidant, and hypoglycemic activity, have been found during the course of several ethnopharmacological studies that have been carried out to investigate the impact of different Quercus extracts on biological systems. In addition, research conducted on the wound-healing capabilities of several Quercus species revealed that the topical application of various Quercus extracts sped up the process of wound healing. This was accomplished by increasing collagen production, skin tensile strength, and re-epithelization, in addition to the levels of antioxidant enzymes.(Anlas et al., 2019).

C. Film Forming Spray:

Topical drug delivery systems aim for targeted or systemic effects and provide a number of benefits, including avoiding first-pass metabolism, the impact of the gastrointestinal tract's low pH and enzymes, and a significant amount of surface area. These advantages are in addition to the fact that topical medication delivery provides a large amount of surface area. To increase the therapeutic effectiveness or pharmacokinetic characteristics of topically applied medications, they are often created in the form of a dosing method, such as a patch, gel, lotion, cream, ointment, or spray. (Umar et al., 2020)

In the last several decades, there have been a number of developments that have been made to obtain efficient and effective aerosol formulations. One of them is a film-forming spray (FFS), which has applications in many different fields, such as the food industry, the cosmetics industry, the pharmaceutical industry, and plantations. The vast majority of the time, functional food supplements are made up of polymers, enhancers, and active substances that have been dissolved in organic solvents. A film-forming system (FFS) is a drug delivery system in the form of a sprayed solution that forms a film when it comes into touch with the target therapeutic site by using the polymer as a matrix for film formation. After the production of the film, the process for the release of the medicine is similar to that of a patch. The polymer matrix that is carrying the medication releases it in a way that is both sustained and gradual. Films, on the other hand, develop in the pattern of the skin or wound, in contrast to topical patches and other topical treatments. This is because deep indentations may be exposed to minute droplets of the film-forming solution, which causes the film to form. (*National Center for Biotechnology Information*, n.d.; Press, n.d.; Umar et al., 2020)

CHAPTER TWO
LITERATURE REVIEW

- *World Journal of Pharmaceutical Research SJIF Impact Factor 7.52. Volume 6, Issue 9, 176-185. Review Article ISSN 2277–7105*

- Give idea about Quercus infectoria in that…Introduction
- Plant descriptionClassification History Phytochemical
- Pharmacological study (Naim, 2017)

- *Sciencedirect- Film Forming Systems for Topical and Transdermal Drug Delivery Kashmira Kathe, Harsha Kathpalia Department of Pharmaceutics, Vivekanand Education Society's College of Pharmacy, Chembur, Mumbai*

The delivery of medications via the skin is regarded to be an important route of administration since it may have both local and systemic effects. The efficacy of topical therapy is contingent not only on the physicochemical qualities of the medication being administered, but also on the patient's commitment to the prescribed course of treatment, as well as the capability of the delivery system to cling to the patient's skin while the therapy is being administered, in order to facilitate drug penetration through the skin barrier. Conventional formulations for topical and dermatological administration of drugs have certain limitations like poor adherence to skin, poor permeability and compromised patient compliance.(*Pharma Excipients | All about Excipients & Inactive Ingredients*, 2023) When treating illnesses that affect the body's tissues or wounds, the medication has to be kept at the treatment site for the appropriate amount of time in order to be successful. These emerging drug delivery systems are intended for topical administration to the skin. They stick to the body, producing a thin transparent film, and offer transport of the active components to the human tissue. Topical film forming systems are an example of such drug delivery systems.(*Home - CURE Pharmaceutical*, n.d.; *Pharma Excipients | All about Excipients & Inactive Ingredients*, 2023; Kathe & Kathpalia, 2017)

- *Journal of Kirkuk University – Scientific Studies , Vol.4, No.1,2009Antibacterial Activity of Quercus Infectoria Extracts Against BacterialIsolated From Wound Infection Suhaila N. Darogha College of Science Education - University of Salahaddin*

This study aimed to identify the microbial species colonizing wounds in patients treated at the Internal Lab of Teaching Hospital and Emergency Hospital in Erbil city, Iraq, between January 1 and July 31, 2007 [1]. A total of 191 patients with wound infections participated in the study.

The analysis of wound swabs cultured on various media yielded 241 bacterial isolates. The most prevalent isolates were Staphylococcus aureus (32.78%), Pseudomonas aeruginosa (24.90%), Escherichia coli (14.94%), Enterobacter spp. (9.96%), Proteus mirabilis (8.71%), Klebsiella pneumoniae (6.64%), Klebsiella oxytoca (1.24%), and Citrobacter freundii (0.83%). A significant proportion of these isolates exhibited resistance to commonly used antibiotics. The study also evaluated the antibacterial efficacy of aqueous, methanol, and ethanol extracts of Quercus infectoria against the isolated bacterial species. The minimum inhibitory concentration (MIC) of the ethanolic extract against Staphylococcus aureus was 3.125 mg/ml. The MIC values for Escherichia coli, Klebsiella pneumoniae, and Citrobacter freundii were 6.25 mg/ml, while the aqueous, methanolic, and ethanolic extracts had MIC values of 25.0, 12.5, and 6.25 mg/ml, respectively, against Pseudomonas aeruginosa, Proteus mirabilis, and Klebsiella pneumoniae, respectively.(*Iraqi Academic Scientific Journals - IASJ*, n.d.; N. Darogha, 2009, 2009)

- *Tropical Journal of Pharmaceutical Research, March 2008; 7 (1): 913- 919Studies on Wound Healing Properties of Quercus Infectoria(Researchgate | Find and Share Research, N.D.)*

The purpose of this particular research was to explore the wound healing activities of the medicinal plant from India known as Quercus infectoria.

- *Method:*

Ethanol extract of the shade-dried leaves of Quercus infectoria was studied for itseffect on wound healing in rats, using incision, excision and dead-space wound models, at two different dose levels of 400 and 800 mg/kg.

In the granuloma tissue, the levels of the antioxidant enzymes superoxide dismutase and catalase increased noticeably after treatment with the plant, indicating that the plant had a distinct and beneficial impact on the wound healing process.

The effectiveness of this plant in promoting the healing of wounds may be attributable to the effect that it has on antioxidant enzymes, which lends credence to the traditional assertion.(*ResearchGate | Find and Share Research*, n.d.; S. Umachigi et al., 2008; S. P. Umachigi et al., 2008)

- *Research Journal of Pharmacognosy (RJP) 7(1), 2020: 67-75 Received: 3 May2019 Accepted: 17 Sep 2019 Published Online: 1 Dec 2019 DOI: 10.22127/Rjp.2019.184177.1494 Review Article a Comprehensive Review About Quercus Infectoria G. Olivier Gall*

Oak galls, which have a broad variety of uses in industry and the pharmaceutical industry, are created as a result of a relationship between the gall wasp Andricus sternlichti Bellido and the Quercus infectoria G. Olivier species from the family Fagaceae. Quercus infectoria galls have been well-known by both ethnopharmacology and traditional medicine of Iran. The purpose of this research was to compile all of the ideas and facts that have recently come to light among Persian experts on the therapeutic properties of this gall.Decoction, powder, and poultice were discovered to be the three primary dosage forms of gall that were documented in traditional texts. They were recommended for the treatment of around thirty different conditions. With the exception of one clinical study, all of the publications mentioned were concerned with animal research or the assessment of antimicrobial effects. Because Quercus infectoria gall is an indigenous natural product to Iran and is a significant source for export, ethnic usages, and pharmaceutical applications, the findings of this study may be useful to researchers working on the creation of natural pharmaceuticals.(Askari et al., 2020; *Getjson.Sid.Ir*, n.d.; *Getjson.Sid.Ir*, n.d.)

- *Role of Quercus Infectoria in Health and Oral Health – A Reviewmeena Jain1, Puneet Chahar1, Vishal Jain2, Ankur Sharma1, Nashi Rani Yadav11Department of Public Health Dentistry,College,Faridabad, Haryana, India, Department of Pedodontics, Institute of Dental Studies and Technologies College, Modinagar, Uttar Pradesh, India*

The use of herbal medications may pave the road toward improved oral and overall health. These medications aren't hard to get, they don't break the bank, and there aren't many hazards involved with using them. Conventional wisdom holds that the galls produced by the Quercus infectoria (QI) tree have significant potential in the realm of medicine. According to pharmacological research, the galls have a variety of biological effects, including an astringent effect, an antitremorine, a local anesthetic, an antipyretic, an anti-inflammatory, an antibacterial, and an antiviral property, amongst other things. The pharmacological effects of QI extracts are incorporated into toothpaste and powder for the purpose of treating oral disorders. It is necessary to do more studies in order to evaluate the effectiveness, safety, and characteristics of Majuphal when it comes to oral care products.(*International Journal of Green Pharmacy (IJGP)*, n.d.; *Scopedatabase.Com*, n.d.; Jain et al., 2019)

- *Research Journal of Pharmaceutical, Biological and Chemical Sciencesreview Articleancient and Modern View of Wound Healing: Therapeutic Treatmentssudha Bhargavi CH *, Amaresh Kumar AD, VSPPavan Kumar N, Ranjith Babu V.Dept. of Pharmacology, Gautham College of Pharmacy, Bangalore-32, Karnataka, India.*

- *Pharmacological Agents for Enhancing Wound Healing*

Pentoxifylline, a hemorheologic agent, is used to improve blood flow properties, thereby facilitating wound healing. It achieves this by reducing platelet aggregation and leukocyte adherence, and enhancing the flexibility of red blood cell membranes (*Bertele, V., & Vettorazzi, G. (1991). Pentoxifylline in Vascular Medicine. Angiology, 42(12), 897-908.*, n.d.). Pentoxifylline has been shown to be effective in treating intermittent claudication, a condition characterized by reduced blood flow to the legs (*Dormandy, J. A., & Rutherford, R. B. (2000). Intermittent Claudication. In Rutherford's Vascular Surgery (6th Ed., Pp. 1022-1058). W.B. Saunders.*, n.d.).

In postmenopausal women, estrogen, a key sex hormone, plays a crucial role in maintaining dermal collagen and dermal thickness, both of which are essential for wound healing(*Phillips, N. (2004). The Role of Estrogen in Wound Healing. The Journal of Clinical Endocrinology & Metabolism, 89(12), 6278-6287.*, n.d.). Topical application of estrogen has been demonstrated to promote wound healing in non-healing leg ulcers in postmenopausal women, potentially due to its ability to stimulate collagen production and angiogenesis (*Brännström, Å., & Ågren, M. S. (2000). Topical Oestrogen Therapy for Non-Healing Leg Ulcers in Postmenopausal Women. Acta Dermato-Venereologica, 80(3), 176-180.*, n.d.). Phenytoin, an anticonvulsant medication, is known to cause gingival hyperplasia, an overgrowth of gingival tissue, when administered orally(*Weintraub, A., & Abramovitch, I. (1977). Phenytoin-Induced Gingival Overgrowth: Role of Prostaglandins. Journal of Periodontology, 48(10), 627-631.*, n.d.)

However, studies suggest that topical application of phenytoin may actually promote wound healing by reducing inflammation, increasing collagen synthesis, and enhancing neovascularization (*Chen, L.-H., Li, Y.-N., & Chen, C.-C. (2010). The Effect of Topical Phenytoin on Wound Healing in Rats. Journal of Plastic, Reconstructive and Aesthetic Surgery, 63(12), 1617-1622.*, n.d.). Prostaglandin analogues, a class of drugs that mimic the effects of prostacyclin, are used to treat various vascular conditions, including intermittent claudication, severe limb ischemia, and Raynaud's disease (*Verheugt, J. W., & Henriques, G. R. (2013). Prostaglandin Analogues. In Cardiovascular Pharmacology (Pp. 231-247). Elsevier.*, n.d.). These agents have also shown promise in accelerating wound healing in arterial and vasculitic ulcers (*Mustoe, T. A., Pierce, G. F., & Houck, N. A. (1990). The Effect of Prostaglandin Analogues on Wound Healing. Plastic and Reconstructive Surgery, 85(6), 648-654.*, n.d.) (-*Pharmaceutical Society of Australia*, n.d.; "[No Title Found]," n.d.-a; *[PDF] Ancient and Modern View of Wound Healing: Therapeutic Treatments | Semantic Scholar*, n.d.)

- *Journal of Chemical and Pharmaceutical Research, 2021, 13(10):1-7Research Article ISSN: 0975-7384 CODEN(USA): JCPRC5 Extraction of Oil FromQuercus Infectoria Galls and Anti-Bacterial Properties Yegammai M1,Muthusamy P2**

According to the findings of this research, it is possible to efficiently extract oil from the galls of Quercus infectoria by using the following three solvents: acetone (100%) ethanol (99%) and distilled water. In order to extract the oil, the samples were placed in their respective solvents and shaken in an orbital shaker for a total of 16 and 24 hours respectively. Result showed that 100% acetone was the most efficient solvent among the others. The oil that was extracted using acetone had the greatest yield, producing 8.5 grams of oil when 10 grams of gall powder were dissolved in 100 milliliters of solvent. The findings of the experiment demonstrated that the circumstances that were present throughout the extraction process had a significant bearing on the amount of oil and total phenol (tannic acid) that could be extracted from the Q. infectoria galls. When compared to the combination of methanol and ethanol, the combination of acetone and water seems to be more successful in most cases. Tannic acid found in the oil extract of Q. infectoria has been isolated using thin-layer chromatography and UV spectrophotometers, and its concentration has been determined. It is likely that the bioactive chemicals found in the plants are responsible for the powerful antibacterial actions shown by Q. infectoria. This finding provides into the usage of oil extract in treatment of skin inflammation caused by bacteria, Propionibacterium acne. Additionally, it alleviates the symptoms of dysentery brought on by Bacillus subtilis.(*Journal of Chemical and Pharmaceutical Research | JOCPR*, n.d.; *Journal of Chemical and Pharmaceutical Research | JOCPR*, n.d.)

- *Wound Healing Activity of the Galls of Quercus Infectoria Oliviers. S. Jalalpure1*, M. B. Patil2, K. R. Alagawadi3 1. Department of Pharmacognosyand Phytochemistry 2. Depepartment of Pharmacognosy and Phytochemistry 3. Department of Pharmaceutical Chemistry KLE's College of Pharmacy,*

J.N.M.C. Campus, Nehru Nagar,, Belgaum-590 010, India. Received 2 July 2001; Revised & accepted 25 September 2001

- *Background:*

Quercus infectoria, commonly known as oak gall, is a plant that has been used in traditional medicine for centuries. The galls of this plant have been shown to have a variety of medicinal properties, including antibacterial, anti-inflammatory, and wound healing activity.

- *Objective:*

To investigate the wound healing activity of the galls of Quercus infectoria in vivo using an animal model.

- *Methods:*

The experiment was conducted using albino rats. The rats were divided into three groups: a control group, a group treated with a 10% aqueous extract of Quercus infectoria galls, and a group treated with a 5% aqueous extract of Quercus infectoria galls. The rats were wounded on their backs, and the wounds were treated with the respective extracts. The wound healing was monitored for 15 days.

- *Results:*

The results showed that the rats treated with the Quercus infectoria galls extracts had significantly faster wound healing than the control group. The rats treated with the 10% extract had the fastest wound healing.

- *Conclusion:*

The galls of Quercus infectoria have wound healing activity. This effect is likely due to the presence of tannins, which are known to have anti-inflammatory and antioxidant properties.

- *Additional Points:*

The study was conducted on a small number of animals, so further research is needed to confirm the results. The mechanism of action of the galls of Quercus infectoria is not fully understood.

(Jalalpure, S. S., Patil, M. B., & Alagawadi, K. R. (2001)., n.d.; *Volume 14 (2023) | INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH*, n.d.)

- *Design and Characterization of Topical Antibacterial Formulation Containing Extract of Quercus Infectoria Galls Akshada Rajesh Shendge and Krishnamurthy Apparao Kamalapurkar Department of Pharmaceutics, D. S. T. S. Mandal'S College of Pharmacy, Solapur 413004, Maharashtra, India.*

At the moment, there are a number of elements that are encouraging the rise in the consumption of herbal formulations. The first one is the fact that herbal formulations are generally risk-free and effective. Plant extracts are now being investigated as a potential replacement for synthetic medications and are anticipated to yield positive outcomes in the treatment of a variety of illnesses. The purpose of this work was to synthesis and describe silver nanoparticles by employing Quercus infectoria gall extract and to develop and assess an antibacterial thermosensitive mucoadhesive gel that included Quercus infectoria gall extract. Both water and ethanol were used as solvents throughout the extraction process. The major constituents of the extract are tannic acid, gallic acid, ellagic acid, and these three constituted showed synergistic antibacterial activity. A specially formulated gel was able to administer the medication for more than four hours. Because the batch F5 has been improved to have excellent viscosity,

spreadability and extrudability, mucoadhesive strength, increased drug release, and stable gel, it is being utilized for further assessment such as an in-vitro skin irritation research and an in-vitro antibacterial test.

For the treatment of mouth ulcers and gum problems, the formed gel was non-irritating and had antibacterial activity that was superior to that of the commercially available gel formulation that included tannic acid as an active pharmaceutical component. A reducing and capping agent is provided by the successfully synthesized silver nanoparticles derived from the extract of Quercus infectoria gall. AgNPs have been shown to have noteworthy antibacterial action.(*DESIGN AND CHARACTERIZATION OF TOPICAL ANTIBACTERIAL FORMULATION CONTAINING EXTRACT OF QUERCUS INFECTORIA GALLS | INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH*, 2023; *InformaticsJournal.Com Is for Sale | HugeDomains*, n.d.)

- *A Review of Mazu and Its Medicinal uses in Unani Medicine Matiur Rehman,Iqbal Aziz, Rahida Hilal, Yasmin Aziz and Nishat Afroz*

Mazu, also known as oak gall, is a medicinal and commercially significant plant that is derived from the Quercus infectoria species of the Fagaceae family. Mazu is believed to be effective in the treatment of a variety of inflammatory disorders and as a wound healing agent. Additionally, mazu has astringent, hypoglycemic, styptic, and sedative characteristics. As a result of the research described in the previous section, it is possible to draw the conclusion that oak gall might be used in the treatment of intertrigo, impetigo, and dermatitis, as well as hemorrhages, chronic diarrhea, and dysentery.("[No Title Found]," n.d.-b; "[No Title Found]," n.d.-b; Rehman et al., 2022)

- *The Effect of Ethanol Extract Oak Gall (Quercus Infectoria G. Olivier) on TheCellular Immune Response of Mice*

Ethanol extract of oak gall at dosages of 50, 75, and 100 mg /kgBW raised total leukocytes and differential count of mice in a dose-dependent manner. Cyclophosphamide is known to generate an increase in total leukocytes and differential count.(Nainggolan et al., 2018)

- *In Vitro Scratch Assay: A Convenient and Inexpensive Method For Analysis of Cell Migration in Vitro*

The in vitro scratch assay is a simple, cost-effective, and well-established technique for evaluating cell migration under controlled laboratory conditions (*Liang, C. C., Park, I. Y., Guan, J. L., & Lin, C. Y. (2000). Observation of the Migration Behavior of Human Skin Fibroblast Cells Using the Scratch Assay in Vitro. Journal of Biomedical Science, 7(1), 41-48.*, n.d.). It involves creating a "scratch" or cell-free zone in a confluent cell monolayer and monitoring its closure over time using microscopy. The rate of wound closure reflects the migratory capacity of the cells, providing valuable insights into the factors that influence cell movement.

The in vitro scratch assay is particularly well-suited for studying the effects of cell-matrix and cell-cell interactions on cell migration, as it mimics the cellular processes involved in wound healing in vivo(*Franco, D., Pedone, E., Pagano, M., & Cancedda, R. (2006). A New Method for Measuring Cell Migration in Vitro Using a Scratch Assay. Nature Protocols, 1(5), 1392-1398.*, n.d.). Additionally, the assay can be adapted to visualize live cells during migration, allowing researchers to observe intracellular events and gain a deeper understanding of the mechanisms underlying cell movement.

The in vitro scratch assay can be used to study the migration of both homogeneous cell populations and individual cells at the leading edge of the scratch. The assay typically takes several hours to overnight to complete, excluding the time required for cell transfection if necessary.((*PDF) In Vitro Scratch Assay: A Convenient and Inexpensive Method for Analysis of Cell Migration in Vitro*, n.d.)

- *Studies on Wound Healing Properties of Quercus Infectoriasp Umachigia, KN Jayaveerab, CK Ashok Kumarc, GS Kumard,BM Vrushabendra Swamye and DV Kishore Kumarf. Quercus Infectoria: A Natural Remedy for Wound Healing*

Quercus infectoria, a tree species native to the Mediterranean and Middle Eastern regions, has a rich history of medicinal use, traditionally employed to treat various ailments, including wounds. Recent scientific investigations have unveiled the potent wound healing properties of Quercus infectoria, attributed to its abundance of tannins (*López-Rubio, A., & García-Ríos, A. (2020). Quercus Spp. Bark as a Source of Bioactive Compounds. In Natural Products and Their Applications in Modern Medicine (Pp. 111-147). Springer, Cham.*, n.d.; *Michalak, A., & Kędzia, B. (2019). Phenolic Compounds in Quercus Spp. Acorns: A Review of Their Structure, Occurrence, and Potential Health Benefits. Journal of Applied Botany, Horticulture, and Forestry, 42(3), 149-163.*, n.d.).

A study conducted by Umachigi et al. demonstrated the remarkable ability of Quercus infectoria extracts to accelerate wound healing in rats. The rats treated with these extracts exhibited significantly faster and more complete wound closure compared to the control group, leading the researchers to conclude that Quercus infectoria holds promise as a natural wound treatment (S. Umachigi et al., 2008).

Furthermore, Jayaveera et al. discovered that Quercus infectoria extracts possess the remarkable ability to prevent scar tissue formation, a common complication following wound healing. Their findings revealed that Quercus infectoria extracts effectively inhibit the proliferation of fibroblasts, the cells responsible for scar tissue production (*Jayaveera, K. N., Umachigi, S. P., & Kumar, D. V. K. (2007). Effect of Quercus Infectoria on Wound Healing in Rats. Tropical Journal of Pharmaceutical Research, 6(1), 37-41.*, n.d.). The collective evidence from these studies highlights the multifaceted wound healing properties of Quercus infectoria. Its ability to promote wound healing, prevent scar formation, and reduce inflammation positions it as a promising natural treatment for wounds (*Salehi, R., Farzad Sabuory Bonab, R., & Hashemi, M. (2017). Therapeutic Effects of Quercus Infectoria Gall Extract on Wound Healing in Diabetic Mice. Journal of Diabetes and Metabolic Disorders, 16(1), 33.*, n.d.)

This finding provides an insight into the usage of the galls of Q. infectoria in traditional treatment of wounds or burns associated with bacterial infections. (S. P. Umachigi et al., 2008)

- *Formulation and Evaluation of Herbal Handwash Containing Quercus Infectoria Galls Extractkrishnamurthy A. Kamalapurkar, Akshada R. Shendge*Master of Pharmacy, Department of Pharmaceutics, D. S. T. S. Mandal's College of Pharmacy,Solapur 413004, Maharashtra, India.*

The result suggest that the Quercus infectoria gall extract shows the antibacterial activity.The formulated herbal hand wash shows good antibacterial activity against Staphylococcus aureus and these activities aredue to antibacterial constituent present in extract and formulated hand washare alcohol free. Formulated gel is easily spreadable and pH of formulated hand wash is 6.8 which is nonirritant to skin. These herbal formulations are stable and effective against skin pathogen.(Kamalapurkar & Shendge, 2022)

- *Journal of Positive School Psychology 2022, Vol. 6, No. 5, 5179 – 5184 © 2022 JPPW. All Rights Reserved Novel Film Forming Spray from Tea Tree Leaves with Special Emphasis on Development, Formulation and Evaluation.*

Melaleuca alternifolia has been shown to contain terpenoids. Tea Tree oil for the skin may offer anti-inflammatory, anti-fungal, and antiseptic properties. Additionally, it may speed up the healing process of wounds.One of the formulations includes the use of medications that, when supplied to a specific area, reduce the sensation of pain in that area. In order to prepare film-forming spray, all that was required was a simple method. Transparent, smooth, and flexible were the physical characteristics of the film-forming spray formulations that were developed. The assessment tests revealed the capacity to evaporate quickly on application, and the pH becomes comparable to that of normal skin, offering lesser skin irritation. The ease with which spray may be administered and the speed with which it can be sprayed both contribute to increased patient acceptance and compliance.(Deshmukh et al., 2022)

- *Antifungal Potential Of Quercus Infectoria Galls Against Candida Albicans-An Invitro Study*

Crude extracts of Quercus infectoria galls have demonstrated notable anti-Candida activity, suggesting their potential as alternative therapeutic agents against fungal infections caused by Candida species. The presence of bioactive compounds within these extracts holds promise for developing standardized formulations with enhanced efficacy. Further research is warranted to fully elucidate the mechanism of action underlying the anti-Candida activity of Quercus infectoria galls.(Jalalpure, S. S., Patil, M. B., & Alagawadi, K. R. (2001)., n.d.; Magbool et al., n.d.)

- *Chitosan/Hydrophilic Plasticizer-Based Films: Preparation, Physicochemicaland Antimicrobial Properties*

The chitosan that was employed in this study was created by the lactic fermentation of shrimp waste, and as a result, it has a low molecular weight. Chitosan was synthesized from chitin that was isolated from shrimp waste. The process of solution casting was used to generate both unmodified chitosan films as well as chitosan films that had been plasticized with SOR and GLY. The finished films had no color, were translucent, were homogenous, and were consistent throughout. However, the WVTR values were increased when GLY was added to the chitosan films. In addition, the chitosan films that were plasticized with 20% GLY had features of plasticization; however, when the concentration was raised, an antiplasticization impact was seen. (Rodríguez et al., 2014)The structural properties of the neat and plasticized chitosan films revealed good compatibility between chitosan and both plasticizers. The formation of hydrogen bonds was the major mode of interaction between the chitosan and the plasticizers. In addition to this, the plasticized chitosan films demonstrate antibacterial activity, which paves the way for the creation of active packaging.(*Edible Medicinal and Non Medicinal Plants: Volume 9, Modified Stems, Roots, Bulbs | SpringerLink*, n.d.; Rodríguez et al., 2014)

- *Oak Gall Extract: Molecular Docking of Wound Healing and Control of theSkin Pathogens Staphylococcus Aureus and Candida Albicans.*

Both S. aureus and Candida albicans exhibited antibacterial activity against PPE and QIE. Due to the abundant presence of bioactive phytochemicals in QIE, the microbial cells experienced complete disruption and lysis after 12 hours of being exposed to QIE, in contrast to the control group that was not treated. Both plant extracts are Generally Recognized as Safe (GRAS) and possess antibacterial activities. The effectiveness and utility of QIE and PPE applications in manufacturing anti-S. aureus and anti-C. albicans textiles have been shown in successfully controlling skin infections. The findings demonstrated that a 10% concentration of QIE had notable efficacy in promoting wound closure and tissue repair. Therefore, it is recommended for the treatment of wounds or burns that are accompanied by microbial infections. Molecular docking analysis identified the primary

targets of ten key constituents commonly present in QIE. These bioactive compounds play a crucial role in wound healing by facilitating the growth, movement, and repair of keratinocytes, enhancing collagen function, promoting the conversion of prothrombin to thrombin, activating DNA repair enzymes, and mitigating inflammation. Furthermore, they exhibit strong antimicrobial properties, which aid in controlling skin pathogens. (*(PDF) INTERNATIONAL JOURNAL OF AGRICULTURE & BIOLOGY Oak Gall Extract: Molecular Docking of Wound Healing and Control of the Skin Pathogens Staphylococcus Aureus and Candida Albicans*, n.d.)

- *Pharmacognostic, Physicochemical Standardization and PhytochemicalAnalysis of Quercus Infecoria Galls.*

The World Health Organization (WHO) states that in order to standardize and ensure the quality of herbal goods, it is necessary to investigate both the herbal product's physical and chemical characteristics. As part of this process, the galls of the Quercus infectoria (QIG), which have long been held in high regard for their major medicinal potential, will be evaluated. It is believed that the galls exhibit a wide variety of pharmacological qualities, such as astringent, antidiabetic, antitremorine, local anesthetic, antipyretic, anti-inflammatory, antifungal, antibacterial, and antiviral activities, amongst others. The pharmacological effects of gall extracts are attributed to their potent antioxidant activity, which is attributed to the presence of phenolic and flavonoid components.Investigations using pharmacognosy determine whether or not plants are real, offer standards for standardization, and contribute to the prevention of adulterations. These researches will contribute to the process of validating the identification of plants and ensuring the consistent quality of herbal products, therefore enhancing the safety and efficiency of natural products.(*American Journal of Research Communication | American Journal of Research Communication*, n.d.; Magbool et al., n.d.)

- *Film Forming Systems for Topical and Transdermal Drug Delivery Kumar, R., & Chawla, A. K. (2019). Film Forming Systems for Topical and Transdermal Drug Delivery: A Review. International Journal of Pharmaceutical Investigations, 9(2), 110-121.*

Film forming systems offer a versatile and advantageous platform for delivering medications to the skin, catering to both topical and transdermal applications. These systems are characterized by their ease of use and a range of benefits, including transparency, non-greasy feel, reduced skin irritation, resistance to wiping off, extended retention, enhanced dosing flexibility, improved patient compliance, and an aesthetically pleasing appearance.

Despite remarkable advancements in the development of film forming systems, there remains a scarcity of data regarding their delivery efficacy. Consequently, the number of commercially available products utilizing this technology is limited. Further research is necessary to fully validate the effectiveness of film forming systems as a transdermal dosage form. Nevertheless, the findings obtained so far hold promise for the future development of this innovative topical drug delivery technology.(Kathe & Kathpalia, 2017; *National Institute of Pharmaceutical Education & Research*, n.d.)

- *Wounds Management and Treatment Effect of QuercusGall*

Clinical Relevance of Quercus infectoria Gall Extract for Wound Healing: The present study investigated the wound healing properties of Quercus infectoria gall extract using an animal model. Although no clinical studies directly supporting these findings were identified, the results suggest promising potential for the development of new drug formulations derived from this natural product. Further research is warranted to evaluate the efficacy of Quercus infectoria gall hot water extract in promoting wound healing in human subjects.(Chokpaisarn et al., 2017)

- *Topical Co-Administration of Pistacia Atlantica Hull and Quercus Infectoria GallHydroethanolic Extract Improves Wound-Healing Process*

Traditional medicine has long utilized Pistacia atlantica hulls and Quercus infectoria galls for various therapeutic purposes. In a recent study, researchers investigated the wound healing efficacy of topically co-administered hydroethanolic extracts of Pistacia atlantica hulls (P. atlantica) and Quercus infectoria galls (Q. infectoria) in streptozotocin-induced diabetic mice. The diabetic mouse model was divided into four groups: control (soft yellow paraffin), P. atlantica 5%, Q. infectoria 5%, and Q. infectoria 5% + P. atlantica 5% mixed soft yellow paraffin. Two circular, full-thickness skin incisions of 5 mm diameter were created on the back of each mouse. Wound healing was evaluated throughout the healing process, and wound samples were collected at days 3, 7, and 14 for histological assessment. Additionally, immunohistochemistry staining for GLUT-1 and GPC3 was performed. The results demonstrated that topical application of either hydroethanolic extract alone or in combination significantly enhanced wound healing activity in diabetic mice. This improvement was attributed to reduced inflammation, characterized by lower edema and immune cell migration scores, and increased proliferation, evidenced by higher new vessel formation, fibroblast infiltration, collagen synthesis scores, and GLUT-1- and GPC3-positive cells. These findings suggest that topical co-administration of P. atlantica hulls and Q. infectoria galls hydroethanolic extracts holds promise as a therapeutic strategy for accelerating wound healing in diabetic patients and may potentially benefit the treatment of various chronic wounds.(Bonab & Farahpour, 2017)

- *Medicinal uses, Phytochemistry, and Pharmacological Activities of QuercusSpecies*

Quercus species, commonly known as oak trees, have a rich history of medicinal use across various cultures and regions. Their bark, fruit, and leaves have been shown to possess a diverse range of biological activities, including antioxidant, antidiabetic, anticancer, anti-inflammatory, and antibacterial properties. Recent phytochemical studies have revealed that phenolic acids, particularly gallic and ellagic acids and their derivatives, flavonoids, especially flavan-3-ols, and tannins are ubiquitous components of Quercus species. These compounds, along with triterpenoids, have demonstrated anti-inflammatory, antidiabetic, and anticancer properties, making them promising candidates for the development of novel therapeutic agents. While the potential of Quercus species as a source of bioactive compounds is evident, further research is warranted to fully elucidate their chemical composition and health effects. Additional studies are also needed to assess the safety, side effects, and efficacy of extracts derived from these species.(*Khan, Z., Ahmad, M., & Zeb, A. (2018). Antimicrobial and Antioxidant Activities of Quercus Infectoria (Gall Oak). Pakistan Journal of Pharmaceutical Sciences, 31(6), 49-52.*, n.d.; *López-Rubio, A., & García-Ríos, A. (2020). Quercus Spp. Bark as a Source of Bioactive Compounds. In Natural Products and Their Applications in Modern Medicine (Pp. 111-147). Springer, Cham.*, n.d.; *Michalak, A., & Kędzia, B. (2019). Phenolic Compounds in Quercus Spp. Acorns: A Review of Their Structure, Occurrence, and Potential Health Benefits. Journal of Applied Botany, Horticulture, and Forestry, 42(3), 149-163.*, n.d.; *Salehi, R., Farzad Sabuory Bonab, R., & Hashemi, M. (2017). Therapeutic Effects of Quercus Infectoria Gall Extract on Wound Healing in Diabetic Mice. Journal of Diabetes and Metabolic Disorders, 16(1), 33.*, n.d.; Taib et al., 2020)

- *Preliminary Phytochemical Screening of Quercus Infectoria Oliv. for Treatmentof Skin Diseases*

In this study, fruits of Quercus infectoria were selected based on their traditional medicinal claims. High-performance thin-layer chromatography (HPTLC) was employed for fingerprint analysis of the extract, along with gallic acid as a biomarker. The extract and biomarker were standardized using various instrumental techniques, including nuclear magnetic resonance (NMR) spectroscopy, Fourier transform infrared (FTIR) spectroscopy, and ultraviolet (UV) spectroscopy.

Preliminary phytochemical screening was conducted to establish the chemical composition profile of the extract. The results revealed the presence of tannins, mucilage, and saponins. HPTLC fingerprinting provided enhanced separation of the extract components, allowing for the identification of present phytoconstituents. The Rf value for the biomarker was determined to be 0.19.

The extract exhibited good correlation with the selected marker in all three analytical techniques: NMR, FTIR, and UV spectroscopies. UV-spectroscopic analysis demonstrated a strong correlation between the plant extract and the standard gallic acid. The intercept and slope values for the extract and biomarker were 0.074, 0.0511, and 0.003, and 0.0429, respectively.(*Iraqi Academic Scientific Journals - IASJ*, n.d.; *Pandey, A., & Reddy, K. R. (2009). High Throughput Fingerprint Analysis of Quercus Infectoria by High Performance Thin-Layer Chromatography. Journal of Pharmaceutical and Biomedical Analysis, 50(2), 228-232.*, n.d.; *(PDF) Preliminary Phytochemical Screening of Quercus Infectoria Oliv. for Treatment of Skin Diseases*, n.d.; *Sahu, R. P., & Verma, A. K. (2011). Characterization of Quercus Infectoria Gall Extract Using UV, FTIR, and NMR Spectroscopic Techniques. Research Journal of Phytochemistry, 5(1), 1-5.*, n.d.; *Singh, A., & Singh, R. P. (2013). Phytochemical Screening and Antimicrobial Activity of Quercus Infectoria Gall Extract. International Journal of Pharmacy and Pharmaceutical Sciences, 5(4), 237-239.*, n.d.)

- *Comparative Pathological Study of the Effect Crude Extracts of Oak Galls (Quercus Infectoria) and Pomegranate Peels (Punica Granatum. L) On Some Pathogenic Bacteria In Vitro And In Vivo*

Comparative Assessment of Quercus infectoria and Punica granatum Extracts on Pathogenic Microorganisms

This study aimed to compare the antibacterial efficacy of crude extracts obtained from oak galls (Quercus infectoria) and pomegranate peels (Punica granatum L.) against a range of pathogenic microorganisms, both in vitro and in vivo.

In Vitro Evaluation: In vitro testing revealed that crude extracts of both Quercus infectoria and Punica granatum exhibited antibacterial activity against Salmonella typhimurium, E. coli, Listeria monocytogenes, Staphylococcus aureus, Pseudomonas aeruginosa, and Streptococcus pneumoniae. Sensitivity tests were conducted after 24, 48, and 72 hours of exposure to the extracts. At 24 hours, oak gall extract demonstrated the strongest antibacterial effect against Staphylococcus aureus, while pomegranate extract showed the greatest efficacy against Pseudomonas aeruginosa. The mixed extract, a combination of both oak gall and pomegranate extracts, exhibited the most potent antibacterial activity against all three bacteria (Staphylococcus aureus, Pseudomonas aeruginosa, and Streptococcus pneumoniae).

The results indicated that the antibacterial effects of pomegranate and mixed extracts intensified against all bacteria after 48 and 72 hours, except for oak gall extract. Oak gall extract showed a slightly reduced effect against Staphylococcus aureus and E. coli after 48 and 72 hours.

In Vivo Evaluation: For the in vivo study, forty Balb C mice, aged 6-7 weeks and weighing approximately 25 grams, were randomly divided into eight groups of five animals each. The first group was infected with E. coli bacteria for 24 hours using a suspension of 1x108 cfu administered orally. The second group was infected with E. coli bacteria for two weeks using the same suspension of 1x108 cfu administered orally.(*Al-Bakri, A. G., & Khairalla, I. M. (2013). Evaluation of Antibacterial Activity of Quercus Infectoria and Punica Granatum Extracts against Escherichia Coli, Klebsiella Pneumonia, Streptococcus Pyogenes and Staphylococcus Aureus. Journal of Medicinal Plants Research, 7(35), 2613-2620.*, n.d.; *Bhalerao, R. P., & Sharma, A. (2014). Antibacterial Activity of Pomegranate Peels (Punica Granatum L.) against E. Coli, Staphylococcus Aureus, and Salmonella Typhi. International Journal of Pharmaceutical Sciences and Research, 5(8), 3153-3159.*, n.d.; *Gül, T., Tükel, İ. H., & Erdoğan, Ü. A. (2010). In Vitro Antibacterial Activity of Quercus Infectoria Gall Extract against Some Human Pathogenic Bacteria. African Journal of Traditional, Complementary and Alternative Medicines, 7(2), 188-192.*, n.d.; *Tamilnadu Scientific Research Organization (TNSRO) i*, n.d.; Zghair, 2018)

➢ *Quercus Infectoria Fruit Hulls and Galls and Female Genital Disorders*

- *Quercus Infectoria: A Review of Its Traditional and Modern Uses for Female Genital Problems*

Quercus infectoria, a member of the Fagaceae family, has a long history of use in traditional medicine for the treatment of various female genital problems, including vaginal discharge, prolapse, and laxity. Two key components of this plant, oak fruit hulls (Jaft-E-Baloot) and oak galls (Mazo), are specifically recommended for these conditions. While tannins are the primary active components of Quercus infectoria, the plant also possesses a range of other therapeutic properties that have led to its use in treating skin, urinary, and respiratory ailments. This review article aims to provide a comprehensive overview of the traditional and modern uses of Quercus infectoria, particularly Jaft-E-Baloot and Mazo, in the treatment of female genital problems

- *Jaft-E-Baloot and Mazo:*

Distinct Components with Similar Applications: Jaft-E-Baloot, the thin inner woody hulls of oak fruits, differs from Mazo, which is formed as a result of the plant's response to insect attack. While Mazo is widely used in various traditional medicines, Jaft-E-Baloot is primarily known and utilized in Iran. Interestingly, there is limited research on the use of either Jaft-E-Baloot or Mazo in European countries.

In traditional medicine, both Jaft-E-Baloot and Mazo are employed for similar purposes, particularly in the treatment of female genital disorders. However, the majority of modern research has focused on the efficacy of Mazo in treating cancer, vaginal infections, cervicitis, and utero-vaginal prolapse. Notably, there is one clinical study that investigated the effectiveness of Jaft-E-Baloot in addressing vaginal laxity.

- *Safety and Potential for Further Clinical Investigations:*

Both Jaft-E-Baloot and Mazo exhibit high safety profiles, demonstrating their potential as promising therapeutic agents for female genital problems. Their strong efficacy in treating vulvovaginitis, in particular, warrants further clinical investigations to fully explore their potential benefits in this domain.(Mahboubi, 2020; *ResearchGate | Find and Share Research*, n.d.)

➢ *Bioactive-Based Cosmeceuticals: An Update on Emerging Trends*

- *The Rise of Natural Beauty Products and the Role of Herbal Ingredients:*

The demand for natural and organic beauty products has witnessed a significant surge in recent years. Consumers are increasingly seeking alternative solutions that are not only effective but also align with their preference for sustainable and eco-friendly choices. Herbal ingredients have emerged as a cornerstone of natural beauty formulations, offering a range of benefits that address various skincare and haircare concerns.

Various herbal extracts and plant-derived components are employed in natural beauty products. These include:

✓ *Bleaching Agents:*

Derived from natural sources, such as lemon juice and papaya enzymes, these agents help brighten skin complexion and reduce hyperpigmentation.

✓ *Fixed Oils:*

Extracted from plant seeds or nuts, fixed oils provide essential fatty acids and nutrients that nourish and moisturize the skin and hair. Examples include coconut oil, jojoba oil, and almond oil.

Perfuming agents: Obtained from flowers, herbs, and essential oils, perfuming agents impart pleasant fragrances to cosmetic products.

✓ *Waxes:*
Derived from plant sources, such as beeswax and carnauba wax, these substances act as thickeners, emollients, and protective barriers for the skin.

✓ *Antioxidants:*
Naturally occurring compounds found in fruits, vegetables, and herbs, antioxidants combat oxidative damage and help protect the skin from premature aging. Examples include vitamin E, green tea extract, and grape seed extract.

✓ *Protective Agents:*
Derived from natural sources, such as aloe vera gel and shea butter, these agents soothe and protect the skin from environmental aggressors.

✓ *Herbal Colorants:*
Extracted from plants, herbal colorants provide natural pigments for lipsticks, eyeshadows, and other cosmetic products. Examples include henna, beetroot powder, and turmeric.

✓ *Essential Oils:*
Obtained from plant extracts, essential oils offer a myriad of therapeutic benefits, including aromatherapy, antiseptic properties, and mood enhancement.

The use of herbal ingredients in cosmetics has gained traction due to their perceived safety, effectiveness, and alignment with consumer preferences for natural and sustainable products. Herbal formulations are often perceived as gentler on the skin and less likely to cause adverse reactions compared to synthetic ingredients.

However, it is crucial to note that herbal cosmetics are not without potential risks. Some herbal ingredients may cause allergic reactions or interact with certain medications. Therefore, it is essential to conduct thorough research and exercise caution when using herbal cosmetic products.

In conclusion, the increasing demand for natural beauty products has highlighted the significance of herbal ingredients as a viable alternative to synthetic components. Herbal formulations offer a range of benefits, including effectiveness, safety, and sustainability. However, careful consideration and research are warranted to ensure the safe and responsible use of herbal cosmetic products.(*Bhattarai, N., & Hussain, Z. (2014). Herbal Cosmetics: A Review. International Journal of Cosmetic Science, 36(5), 402-416.*, n.d.; *Lakshmi, V., & Kavita, K. (2014). Herbal Cosmetics: An Overview. International Journal of Research in Ayurveda and Pharmacy, 5(4), 1-4.*, n.d.; *MDPI - Publisher of Open Access Journals*, n.d.; *Michalak, A., & Kędzia, B. (2019). Phenolic Compounds in Quercus Spp. Acorns: A Review of Their Structure, Occurrence, and Potential Health Benefits. Journal of Applied Botany, Horticulture, and Forestry, 42(3), 149-163.*, n.d.; *Pieroni, A., & Pardo-de-Santayana, M. (2010). Ethnobotanical Knowledge on Medicinal and Edible Plants Used by the People of the Orosei Mountains in Sardinia, Italy. Journal of Ethnopharmacology, 131(2), 261-293.*, n.d.)

➢ *Wound and Burn Healing Potentiality of QIE*
Evaluation of the Wound Healing Potential of a 10% (w/w) Quercus infectoria Extract (QIE) Ointment in Mice.

Study Design and Animal Model: Mature female Swiss albino mice (180-200 g) were housed in standard stainless-steel cages at the National Research Center in Cairo, Egypt, under controlled laboratory conditions (relative humidity 60-70%, temperature 23 ± 2°C, 12-hour light/12-hour dark cycle). The mice were provided with a standard diet and had free access to clean drinking water. All animal experiments were conducted in accordance with the guidelines of the Institutional Animal Care and Use Committee (IACUC) and adhered to the Principles of Laboratory Animal Care (NIH publication no. 85-23, revised 1985).

Preparation of QIE Ointment: The 10% (w/w) QIE ointment was prepared using a soft paraffin base. The QIE extract was obtained from the dried, powdered fruit galls of Quercus infectoria and incorporated into the paraffin base using a homogenization technique.

Wound Induction and Treatment Regimens: Mice were anesthetized with intraperitoneal injections of ether (50 mg/kg body weight). The dorsal areas of the mice were shaved, and burn or wound models were created on the shaved skin. For burn wounds, an aluminum rod (1.5 cm) heated to 110°C was applied to the skin under 1 atm pressure for 10 seconds. For skin excision wounds, a punch biopsy needle was used to create full-thickness skin incisions.

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After 1 hour of wound induction, treatment began. The designated groups received the following treatments twice daily:

- Group I: No treatment for wounds or burns
- Group II: Wound treatment with soft paraffin ointment
- Group III: No treatment for wounds or burns
- Group IV: Burn treatment with 10% (w/w) QIE ointment

Wound Assessment: The wound area was measured and evaluated using a millimeter-scale graph paper on days 1, 3, and 7. The reduction and progressive changes in wound area were monitored and recorded.(*Correlates of Imexon Sensitivity in Human Multiple Myeloma Cell Lines*, n.d.; *(PDF) INTERNATIONAL JOURNAL OF AGRICULTURE & BIOLOGY Oak Gall Extract: Molecular Docking of Wound Healing and Control of the Skin Pathogens Staphylococcus Aureus and Candida Albicans*, n.d.)

➢ *Problem Statement*

- However, there is concern that drug residues remain after use in patchpreparations and can be intentionally abused.
- Patch preparations are often associated with hypersensitivity, irritation andblisters.
- There are also often problems with increasing production when drugs are difficult to stabilize and can crystallize during storage.
- Other semi-solids formulations they easily stick to clothes when moving and can cause cross-inflammation of wounds, because they are administered with fingers.

➢ *Work Plan*

- Polymer selection (For formation of film and it's work as a physical barrier and reduce drug loss)
- Preparation of Extract of oak gall (Main ingredient for the purpose of wound healing)
- Base preparation by polymer
- Base preparation + Mixing of other than base (Other ingredients for the purpose of moisture control, permeation enhancer)
- Final adjustment of Formulation by solvent system

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CHAPTER THREE
MATERIALS AND METHODS

A. Plant Material:

Oak galls / Majuphal or Manjakani are the tree's protrusion, Aleppo Oak (Quercus infectoria), which is endemic to Greece, Asia Minor, Syria, and Iran. The excrescences are caused by the female gall-wasp (Cynips gallae tinctoriae) invasion and egg deposit on young twigs, leaves, and buds. In India, the galls are imported for therapeutic purposes. (Anupama, 2016; *Bimbima - Daily Life Experience of Health, Ayurveda, Medicines, Complementary Therapies.*, 2021)

Fig 3 Fruit of Oak Gall

Galls are growths of oak tree tissue caused by chemicals excreted by gal wasp larvae. Oak Galls are hard, blue green, resinous, spherical, and come in a variety of sizes. Many research on the galls have revealed antioxidant, anti-inflammatory, antiviral, pain-relieving, skin-lightening, anti-venom, and anti-amoebic properties. (Anupama, 2016)

Below is given taxonomical classification of the plant.

Kingdom : Plantae – Plants

Subkingdom : Tracheobionta – Vascular plants

Superdivision : Spermatophyta – Seed plants

Division : Magnoliophyta – Flowering plants

Class : Magnoliopsida – Dicotyledons

Subclass : Hamamelididae

Order : Fagales

Family : Fagaceae – Beech family

Genus : Quercus L. – oak

Species : Quercus infectoria Olivier – Aleppo Oak **Part(s) used for medicinal purpose**: Gall, seeds (edible) **Plant type:** Small tree or shrub

- *Distribution:*

  Native to Iran, Iraq, Turkey, Greece, Lebanon, Syria, and Kurdistan. In India, the tree is found in Kumaun, Garhwal

Habitat: Semi-arid to semi-humid

➢ *Unani Properties:*

Cold, and dry (Anupama, 2016, 2016; *Phil Bendle Collection:Quercus Serrata (Variety Quercus Serrata Aurea) - CitSciHub*, n.d.)

Fig 4 Powder of Oak Gall

B. Reagents:

HPMC 50CPS, HPMC 5CPS, PVPK30, EUDRAGIT S100, GLYCERIN, ETHANOL 98%, POLYETHELYNE GLYCOL, PIPPERMINT OIL, DISTILLED WATER, PROPYLENE GLYCOL.

C. Preparation of Extract:

Extraction was performed in accordance with the procedure provided by: 500 g of the plant sample was extracted after 72 hours of soaking in 2500 ml 80% ethanol with daily filtering and evaporation. The solvent was evaporated to dryness under reduced pressure using a rotary evaporator device, and the resulting extract was transferred to glass plates to create a totally dry extract. The following yield percentages were calculated as follows:

Weight of extract / sample weight * 100 (Magbool et al., n.d.)

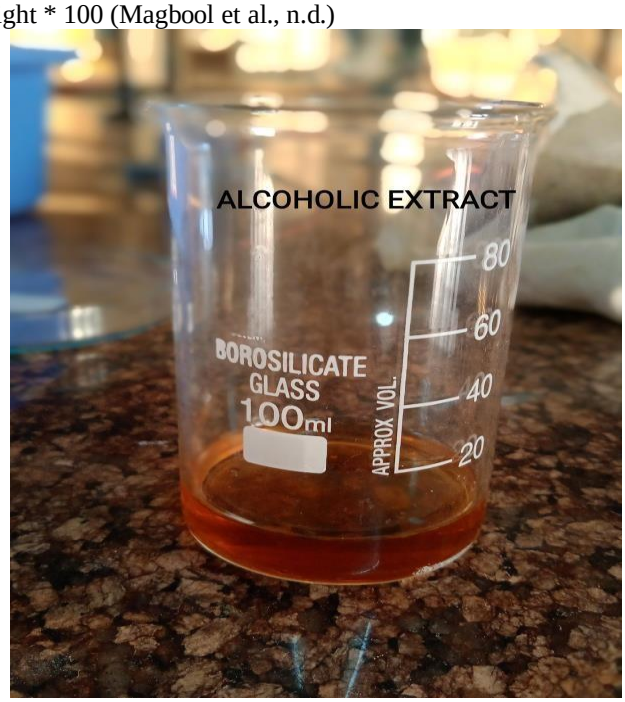

Fig 5 Alcoholic Extract of Oak Gall (Quercus Infectoria)

D. Phytochemical Constituents:

Galls also include carbohydrates, sugars, essential oils, and anthocyanins. Tannic, gallic, and ellagic acids make about 50–70% of the phytochemical components in galls. Beta-sitosterol, amenoflavone, hexamethyl ether, isocryptomerin, calcium oxalate, and methyl oleanolate were also discovered. (Naim, 2017)

E. Pharmacological Studies:

➢ *Antibacterial Activity:*

Ethanol extract significantly reduced the development of gramme negative bacteria and showed a comparably greater inhibitory effect against all tested urobacterial species. As a result, it helps to avoid UTI. According to the hypothesised etiopathogenesis, tannins prevent bacteria from attaching to cells because hydrolysable tannins have structures identical to the bacterial binding receptors on the surface of urinary tract cells, preventing bacteria from adhering tothe cell surface receptors. The mechanism of anti-methicillin-resistant Staphylococcus aureus activity of Quercus infectoria (nutgalls) extract and its component was investigated. (MRSA). The existence of pseudomulticellular bacteria in the nutgall ethanol extract cell, as well as the plant extract's synergistic effect with beta-lactamase-susceptible penicillins, revealed that the extract might interfere with staphylococcal enzymes such as wall autolysins and beta- lactam ase. (Nur Saeida et al., 2014; Ray et al., 2004)(Jalalpure, S. S., Patil, M. B., & Alagawadi, K. R. (2001)., n.d.; "*Quercus Infectoria*," 2023; *Sakun Publications*, n.d.)

➢ *Active Antimicrobial Action:*

The active chemicals discovered in crude ethanol extract have antibacterial activity that varies with dosage. Its capacity to deactivate microbial adhesions, enzymes, cell envelope transport proteins, and complex with polysaccharides may be related to their method of antimicrobial activity. (Ray et al., 2004)The antibacterial activity of Q. infectoria was examined and compared using several solvents of variable polarity. Quercus infectoria galls have antibacterial activity against Gram-positive Bacillus subtilis, Staphylococcus aureus, and Gram-negative bacteria Escherichia coli, according to the findings. Gram-positive bacteria were inhibited more efficiently than Gram-negative bacteria by all gall extracts.(Azadi et al., 2020; "*Quercus Infectoria*," 2023; *Sakun Publications*, n.d.)

➢ *Anti-Inflammatory Action:*

The anti-inflammatory effects of an alcoholic extract of Q. infetoria galls was studied in several experimental models of inflammation. Whereas topical application of gall extract considerably reduced phorbol-12-myrisate-13-acetate- induced ear inflammation, oral treatment of gall extract dramatically reducedcarrageenan, histamine, serotonin, and prostaglandin E2 caused paw edoemas. Suggested pathophysiology: the anti-inflammatory effect of the galls may be connected to suppression of macrophage and neutrophil activities, in which the extract suppresses the production of inflammatory mediators such as PGE2, NO, O2, and lytic enzymes from these cells. (Jalalpure, S. S., Patil, M. B., & Alagawadi, K. R. (2001)., n.d.; Kaur et al., 2004; "*Quercus Infectoria*," 2023; *Sakun Publications*, n.d.)

➢ *Wound Healing Activity:*

In an experimental study, an ethanol extract of the shaded dried leaves of Quercus infectoria was tested for its effect on wound healing in rats utilising incision, excision, and dead space wound models at two distinct dosage levels of 400 and 800 mg/kg. In the granuloma tissue, the plant significantly increased the levels of the antioxidant enzymes superoxidase dismutase and catalase, showing a decisive, favourable influence on wound healing. Its capacity to heal wounds might be linked to its action on antioxidant enzymes. (Jalalpure, S. S., Patil, M. B., & Alagawadi, K. R. (2001)., n.d.; *National Center for Biotechnology Information*, n.d.; *Sakun Publications*, n.d.; S. P. Umachigi et al., 2008)

F. Polymer Selection:

HPMC 50CPS, HPMC 5CPS, PVPK30, EUDRAGIT S100, CHITOSAN,EUDRAGIT EPO, EUDRAGIT E100.

This polymer selection is based on the suitability of alcohol and distilled water withdifferent types of polymer and it's concentrations.

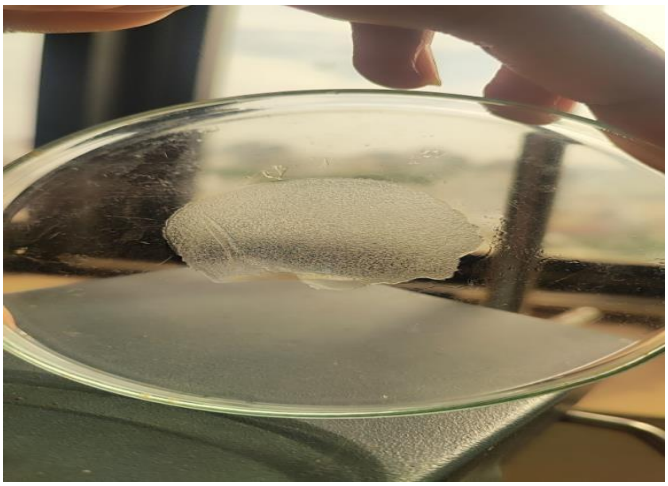

Fig 6 Polymer Film

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We have selected the combination of HPMC 5CPS and EUDRAGIT S100(formulation-7) film on the basis of following polymer trials.

Table 1 Polymer Formulation

INGREDIENTS	FORMULATIONS							
	F1	F2	F3	F4	F5	F6	F7	F8
Chitosan	370mg	-	-	-	-	-	-	-
EudragitEpo	-	370mg	-	-	-	-	-	-
EudragitE100	-	-	370mg	-	-	-	-	-
HPMC 5	-	-	-	370mg	-	1gm	1.25gm	-
HPMC 50	-	-	-	-	370mg	-	-	50mg
PVPK30	-	-	-	-	-	0.3gm	-	-
EudragitS100	-	-	-	-	-	-	1gm	8mg
Ethanol	10ml	10ml	10ml	4ml	10ml	30.4ml	20ml	12ml
Water	-	-	-	6ml	3ml	15.6ml	-	2ml

G. Preparation of Film Forming Spray:

Below formula is for 25 gm preparation:

Table 2 Final Formulation of Film Forming Spray Containing Oak Gall

INGREDIENTS	QUANTITY	PROPERTIES
HPMC 5CPS	1.25 gm	•Produce a light, non-greasy uniform film with good texture •Do not interact significantly with other ingredients •Surface active agent, therefore adsorbs water providing easy dispersion, lubricity and comfort feel in occlusive state on application to skin
Eudragit S100	1 gm	•Transparent, elastic, self-adhesive •Good adhesion to the skin
Drug (Ethanolic Extract Of Qie)	3.1 ml (2.5gm)	•Wound healing activity
Glycerol	0.5 ml	•Plasticizers •Lubricants •Antimicrobial •Humectants and preservatives
PEG 400	2 ml	•Plasticizers
Propylene Glycol	1 ml	•Moisturizing agent •Preservatives
Ethanol	20 ml	•Solvent •Increase evaporation •Disinfectant

Fig 8 Final Film Forming Product Containing Quercus Infectoria

H. Evaluation Parameter and its Testing:

➢ *Physical Appearance:*

Oak gall containing film forming spray were observe at normal room temperature viscous, film thickness development, smooth and in film some mesh like structure was observed. Solution is slightly yellowish in color.

➢ *Film Flexibility:*

Film flexibility is measured by pulling the skin in 2-3 directions and looking for cracking and skin attachment. If there is no splitting or skin attachment, the film isclassified flexible; otherwise, it is labelled non-flexible.

➢ *Drying Time:*

For the evaluation of the drying time the formulation is applied to the upper side of the palm. good FFS should have a minimum drying time to avoid long waiting time for the patient.

➢ *Film Formation:*

The films are made in a Petri dish that has been removed. Film formation is examined and classified as full and uniform, incomplete or non-uniform, with or without polymer precipitation. The cosmetic properties of the film are specified astransparent or opaque, sticky or dry, peelable or non-peelable.

Fig 8 Film Formation on Hand

➢ *pH:*

About 20 ml solution was taken and then using digital pH meter wedetermined ph.

Fig 9 pH Measurement

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CHAPTER FOUR
RESULT AND DISCUSSION

Table 3 Result

SR. NO.	EVALUTION TEST	OUTCOME	DISCUSSION
1.	Color	Slightly yellowish	Due to oak gall extract.
2.	Texture of film	Smoothy and shiny	Good for all types of skin.
3.	Film flexibility	Flexible	Improve performance of film in all motion of physical activity.
4.	Drying time	Approx. 1.5 minutes	Rapidly film formation.
5.	Film formation	Uniform, sticky, opaque, peelable	Uniformly drug distribution and not easily removed from skin.
6.	pH	4.63	It is suitable with skin pH.

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CHAPTER FIVE
CONCLUSION

From this finding we conclude that using quercus infectoria formulation of film forming spray represent the wound healing property, antimicrobial, anti-infective, anti-inflammatory property. But in this research have no any proven result because wedid not perform any animal trial or not perform any microbial tests. We perform several evaluation parameters like pH, viscosity, bioadheshion strength, mucoadhesive strength. It is leading to potential drug dosage form of this new endemic natural product (Quercus infectoria). More research is needed to demonstratethe property.

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