IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Review On Wound Healing Properties Of Herbal Hydrogel Patch

[1]Gaurav Vikas Patil, Author, [2]Mr. Amol B. Chaudhary & [3]Dr. Amol. D. Landge

Shram Sadana Bombay Trust Institute of Pharmacy, Jalgaon, India

Abstract: Hydrogel herbal patch combines the beneficial properties of hydrogels, such as biocompatibility and controlled drug release, with the therapeutic potential of herbal extracts. These patches are designed for topical application, offering a moist wound. healing environment and delivering active herbal compounds directly to the affected area. They can be particularly useful for treating wounds, skin conditions, or delivering localized drug therapies. Hydrogel herbal patches represent a convergence of two promising fields: hydrogel technology and herbal medicine. Hydrogels, with their ability to absorb large amounts of water and form a gel-like structure, they provide an ideal environment for wound healing. by maintaining moisture and facilitating nutrient exchange. Furthermore, their biocompatibility and capacity for controlled drug release makes them suitable for delivering therapeutic substances directly to the site of application.

Key words: Hydrogel Patch, Chitosen, Polyvinyl Alcohol, Polyethylene Glycol, etc.

I. INTRODUCTION

A wound healing patch is a dressing to promote tissue repair and regeneration of an incorporating advanced material and technologies.

This patch can be made from various materials including hydrogel, chitosan and other biomaterials and may include feature like delivery systems, antimicrobial agents, and sensors for monitoring wound healing.

What is wound healing?

The wound healing is a natural process of repairing damage tissue or recovering the injury of cell. It is complex interplay of cellular and molecular event.

Wound healing involves four main stages(phases) =

1. Homeostasis
2. Inflammation
3. Proliferation
4. Maturation (Remoulding)

1. **Homeostasis:**

This phase begins immediately after injury, where the body's initial response is to stop bleeding. Platelets aggregate to form a plug, and blood vessels constrict to reduce blood loss.

2. **Inflammation:**

Following homeostasis, the inflammatory phase begins. This phase involves the influx of white blood cells to the wound site to clear debris and fight infection. Neutrophils and macrophages play key roles in this process.

3. **Proliferation:**

In the proliferation phase, new tissue is formed. Fibroblast migrates to the wound, lay down collagen to create a matrix, and blood vessels form to supply nutrients and oxygen.

4. **Remodelling:**

The final phase involves the remodelling of the newly formed tissue. Fibroblasts differentiate into myofibroblasts, which contract to reduce the wound size. Collagen fibres are reorganized, and the scar matures.

Factors Affecting Wound Healing:

- **Age:** Wound healing tends to slow down with age.
- **Nutrition:** Adequate nutrition, including sufficient protein, vitamins, and minerals, is essential for proper healing.
- **Infection:** Bacterial infection can significantly delay or impair wound healing.
- **Medical Conditions:** Conditions like diabetes, obesity, and circulatory problems can negatively impact wound healing.
- **Medications:** Certain medications, such as immune suppressants and some anti-inflammatory drugs, can affect the healing process.

The product which is used in a treatment of wound healing is as follows =

1. Wound healing cream
2. Wound healing patch
3. Wound healing bandages

- Wound Healing Patch =

A wound healing patch is a dressing to promote tissue repair and regeneration of an incorporating advanced material and technologies.

This patch can be made from various materials including hydrogel, chitosan and other biomaterials and may include feature like delivery systems, antimicrobial agents, and sensors for monitoring wound healing.

MATERIAL & METHOD

The Following ingredients are used for formulation of hydrogel patch =

1. Polyvinyl alcohol
2. Polyethylene glycol
3. Chitosen
4. Alginate
5. Sesame oil
6. Mint
7. Bermuda grass juice
8. Marigold petal
9. Hibiscus leaves
10. Yashti
11. Sada Phul flower
12. Camphor
13. Amla leaves
14. Mango Turmeric

Information regarding following components =

AMLA LEAVES (Embolic officinalis leaves)

Family: Phyllanthocin family

Biological Source: Phyllanthus embolic

Description: The biological source of amla leaves is the tree Phyllanthus embolic, also known as Embolic officinalis, which belongs to the Euphorbiaceous family. This tree, commonly called the Indian gooseberry, is native to Southeast Asia and is a rich source of various beneficial compounds, including tannins, flavonoids, and alkaloids, with its leaves being used in traditional medicine and herbal formulations.

Active Component: ascorbic acid, Vitamin-C, Tannis.

Extraction: When we dry the amla leaves in the oven 30 to 45 min and naturally dry the leaves under the shade for 1 to 2 days, then make a powder of it with the help of mixer.

Wound healing mechanism of amla leaves:

Amla leaves promote wound healing by reducing inflammation, accelerating cell proliferation and tissue regeneration, and strengthening the tissue through enhanced collagen cross-linking. Key compounds like gallic acid and tannins contribute to these effects by providing antioxidant activity and supporting the formation of new blood vessels and fibrous tissue.

Properties: Antioxidant properties, Anti-diabetic**,** Anti-inflammatory properties, Analgesic and Antipyretic properties

TURMERIC (ambi halad) (mango ginger):

Family: Zingiberaceae

Biological Source: Curcuma amada.

Ambi Haldi's biological source is the rhizome of Curcuma amada (family Zingiberaceae), a plant known for its raw mango flavor, used culinarily and in traditional medicine. While specific wound healing mechanisms for C. amada itself are not detailed, its close relative turmeric (Curcuma longa) accelerates healing by promoting inflammation, collagen production, and re-epithelialization, and has antibacterial and antioxidant properties. Ambi Haldi is traditionally applied as a paste to treat wounds and skin ailments, and is believed to possess anti-inflammatory, antioxidant, and antimicrobial activities that contribute to wound healing.

Uses:

Culinary: Used in pickles, chutneys, and other dishes for its unique raw mango flavor.

Medicinal:

- Traditional Uses: Applied as a rhizome paste to heal wounds, cuts, and itching, and for skin diseases and sprains.
- Properties: Possesses antioxidant, antimicrobial, and anti-inflammatory properties.

Properties: Antibacterial, Anti-inflammatory, Antioxidant, Phytochemicals:

HIBISCUS LEAVES:

Biological Source: Hibiscus rosa-sinensis.

Family: Malvaceae

Hibiscus leaves, primarily from Hibiscus rosa-sinensis, are in the family Malvaceae and are used for their wound-healing properties, which are attributed to bioactive compounds like flavonoids, tannins, and terpenoids. The leaves' mucilage content and the extract's ability to promote fibroblast activity, collagen synthesis, and epithelial cell migration accelerate wound healing by increasing tensile strength, wound contraction, and granulation tissue formation.

Uses

- Name Wound Healing: The leaves are used to treat and accelerate the healing of wounds, ulcers, and skin injuries.
- Other Uses: Hibiscus also possesses anti-inflammatory, antioxidant, antibacterial, and antifungal properties, and is used in traditional medicine for fever, cough, diabetes, and other conditions.

Properties

- Rich in Mucilage: The leaves contain a significant amount of mucilage, which can contribute to wound healing by providing a protective and hydrating layer.
- Bioactive Compounds: Extracts of hibiscus leaves are rich in bioactive compounds, including flavonoids, tannins, terpenoids, and alkaloids.
- Antioxidant Activity: The presence of flavonoids and other compounds contributes to the plant's antioxidant properties.

Mechanism of Wound Healing

- Increased Fibroblast and Collagen Synthesis: Hibiscus leaf extracts stimulate fibroblasts to produce more fibronectin and collagen, essential components of the extracellular matrix (ECM) that strengthen tissues and promote repair.
- Enhanced Epithelialization: The extract promotes the migration and proliferation of epithelial cells, which are crucial for covering and closing the wound surface.
- Improved Wound Contraction: By enhancing fibroblast activity and their ability to generate force, the extract facilitates wound contraction, which helps to reduce the wound area.
- Increased Granulation Tissue Formation: In wound models, hibiscus extract increased the formation of granulation tissue, indicating improved healing processes.
- Increased Tensile Strength: Wounds treated with hibiscus extract show significantly higher breaking strength, demonstrating improved tissue integrity.
- Hydration: The extract can increase the expression of genes involved in skin hydration, such as aquaporin 3, which improves the overall healing process by supporting cell migration and function.

Extraction or Main Use of leaves:

If we dry the leaves in the presence of sunlight, then the dry leaf is occurred and it avoid the growth of any kind of micro-organism in it and then make a powder of the leaves with the help of mixer which increase the self-proliferation and collagen proliferation and collagen synthesis at the wound site as evidences increases in DNA total protein and total collagen content of granulation tissue. The extract treated wound were found to heal much faster as indicated by improve rate of epithelization and wound contraction.

MINT (PUDINA):

Biological Source: Fresh or dried leaves of plants belonging to the Mentha genus.
Family: Lamiaceae.

Mint leaves' biological source is the Genus Mentha, family Lamiaceae, and common scientific names include Mentha spicata (spearmint) and Mentha piperita (peppermint). They possess antioxidant, antimicrobial, and anti-inflammatory properties, used in food, pharmaceuticals, and traditional medicine. Key constituents are essential oils (menthol, carvone, limonene) and phenolic compounds. Their antimicrobial mechanisms involve disrupting microbial membranes, while anti-inflammatory and antioxidant effects contribute to wound healing.
Properties: Antioxidant, Antimicrobial, Anti-inflammatory, Carminative & Antispasmodic.

Mechanism of Wound Healing The therapeutic effects of mint in wound healing are attributed to several mechanisms:

- Antimicrobial Action: Mints can disrupt the cell membranes of microbes, preventing infections that could hinder healing.
- Anti-inflammatory Effects: Compounds in mint reduce inflammation at the wound site, creating a more favorable environment for tissue repair.
- Antioxidant Activity: By combating oxidative stress, mints protect new cells and support the overall healing process.
- Fibroblast Stimulation: Studies on topical M. piperita essence have shown increases in fibroblasts, a crucial cell type for connective tissue and wound repair.

Extraction:

The powder obtained directly by the dried leaves of mentha.

Main use in formulation:

Menthol having ability to activate cold receptors in the skin and mucous.

MARIEGOLD FLOWER (Genda):

Name: Calendula marigold (Calendula officinalis)
Family: Asteraceae

The Marie Gold flower, or calendula marigold (Calendula officinalis), is in the Asteraceae family and is known for its wound healing properties due to anti-inflammatory and antimicrobial compounds like flavonoids, triterpenoids, and carotenoids. It accelerates tissue regeneration by improving blood flow and stimulating fibroblast activity while reducing inflammation and providing antioxidant protection. It is used in various forms (creams, tinctures, ointments) to treat skin conditions, wounds, burns, and other dermatological issues.

Biological Source

Description: A common ornamental and medicinal herb with yellow and orange flowers.

Uses

Topical Application: Used in creams, ointments, and tinctures for skin conditions such as wounds, abrasions, and burns.

Internal Use: A decoction can be used for internal infections of mucous membranes.

Cosmetic Industry: Utilized in various cosmetic products for its nourishing and soothing effects on the skin.

Minimize the burn: Mariegold has a long history of use in traditional medicine for treating skin condition like burn wound and irritation.

Properties: Anti-inflammatory, Antimicrobial, Antioxidant, Cytotoxic and Antitumor

Chemical Constituents

Flavonoids: Contribute to antioxidant and anti-inflammatory actions.

Triterpenoids: Known for anti-inflammatory and wound-healing properties.

Carotenoids: Pigments like lutein and zeaxanthin that are antioxidants and contribute to anti-inflammatory effects.

Saponins: Also known for anti-inflammatory and wound-healing properties.

Phenolic Acids and Essential Oils: Other compounds present with various bioactive properties.

Polysaccharides: Contribute to the plant's antioxidant and wound-healing effects.

Mechanism of Wound Healing

1. Enhanced Blood Flow: The extract is believed to increase blood flow to the wound area, ensuring an adequate supply of oxygen and nutrients needed for tissue regeneration.
2. Stimulated Fibroblast Activity: Calendula positively influences the generation of new cells, particularly fibroblasts, which are crucial for wound repair and tissue formation.
3. Reduced Inflammation: Flavonoids and triterpenoids in the extract suppress inflammation by inhibiting inflammatory mediators like cytokines and macrophages.
4. Cell Proliferation: The extract promotes the proliferation and migration of skin cells, accelerating the healing process.
5. Antioxidant Protection: Its antioxidant compounds protect the recovering tissues from oxidative stress, which is important for optimal healing.
6. Pigmentation: The caratonoid in mariegold are used to enhance the colour of wound affected skin.

Extraction: The extraction of mariegold flower is occurred by simply drying the flower in the presence of sunlight for 2 to 5 days and then makes a powder of it.

Use of Mariegold in formulation: In essence of mariegold multifaceated action help to create conducive environment for skin regeneration leading to faster and more effective healing of burn wound.

Sesame oil:

Biological Source: Seeds of Sesamum indicum L.

Family: Pedaliaceae

Sesame oil, derived from the biological source Sesamum indicum L., belongs to the Pedaliaceae family and is rich in unsaturated fatty acids and antioxidant compounds like sesamol, sesamin, and sesamolin. Traditionally used in Ayurvedic and Chinese medicine, it possesses anti-inflammatory, antioxidant, and antimicrobial properties that facilitate wound healing by controlling inflammation, promoting tissue repair, and protecting against oxidative stress. Its effectiveness is attributed to a complex mix of phytochemicals that support cellular function during the wound healing process, although human research is limited.

Uses

- Traditional Medicine: Used topically and orally in ancient Chinese medicine and Ayurveda for promoting healing in burns and other wounds.
- Cosmetic: Employed in traditional practices like abhyangam, a type of Ayurvedic massage.
- Nutritional: A healthy source of fat, protein, carbohydrates, vitamins, and minerals, with high amounts of unsaturated fatty acids.

Properties

Anti-inflammatory, Antioxidant, Antimicrobial

Nutritional: Rich in beneficial compounds like phenolic acids, flavonoids, tocopherols, phospholipids, and lignans.

Chemical Constituents

- Phenolic Compounds: Phenolic acids and their derivatives, such as sesamol (SM).
- Flavonoids: A class of plant pigments with antioxidant and anti-inflammatory properties.
- Lignans: Unique compounds like sesamin and sesamolin, known for their health benefits.
- Fatty Acids: Approximately 87% unsaturated fatty acids, including linoleic acid.
- Other: Tocopherols and phospholipids are also present.

Mechanisms of Wound Healing/Main use in formulation:

- Antioxidant Action: Compounds like sesamol neutralize free radicals generated during the wound healing process, preventing cellular damage and promoting a healthy healing environment.

- Anti-inflammatory Effect: The oil helps to modulate the inflammatory response, ensuring it remains controlled and effective for tissue repair.
- Antimicrobial Activity: By inhibiting bacterial growth, it helps to prevent infection in the wound, a crucial factor for successful healing.
- Tissue Regeneration: Its rich nutritional profile and bioactive compounds support the proliferation of fibroblasts and other cells necessary for tissue regeneration and the formation of new tissue.

Methods for the preparation of patch

Hydrogel patches are created through a process involving polymer chemistry and material science. Generally, it involves dissolving polymers in a solvent, mixing in active ingredients, and then inducing a crosslinking reaction to form a gel. The resulting hydrogel is then shaped, dried, and may be sterilized before being incorporated into a patch.

Here's a more detailed breakdown of the process:

1. Polymer Selection and Preparation:

Choosing the right polymer(s):

The type of polymer dictates the hydrogel's properties (e.g., biodegradability, mechanical strength, swelling capacity). Common examples include poly (vinyl alcohol) (PVA), poly(ethylene glycol) (PEG), alginate, and chitosan.

Dissolving the polymer(s):

The chosen polymer(s) are dissolved in a suitable solvent, often water, to form a liquid solution.

2. Incorporation of Active Ingredients:

Adding active compounds:

If the hydrogel patch is intended for drug delivery or other therapeutic purposes, the desired active ingredients (e.g., drugs, growth factors, antimicrobial agents) are added to the polymer solution and mixed thoroughly.

Nanoparticle incorporation:

Nanoparticles, like silver nanoparticles for antibacterial properties, can be incorporated to enhance the hydrogel's functionality.

3. Crosslinking and Gelation:

Crosslinking mechanism:

Crosslinking is the process that turns the polymer solution into a gel. This can be achieved through various methods:

Chemical crosslinking: Using crosslinking agents (e.g., glutaraldehyde, carbodiimide) that form covalent bonds between polymer chains.

Physical crosslinking: Relying on non-covalent interactions like hydrogen bonding or ionic interactions.

Radiation crosslinking: Using high-energy radiation like gamma rays to initiate crosslinking.

Thermal crosslinking: Heating a solution to induce crosslinking, as seen with gelatin.

Gel formation:

The crosslinking reaction results in the formation of a three-dimensional network, trapping the solvent and active ingredients within, thus creating the hydrogel.

4. Shaping and Processing:

Casting or Molding:

The hydrogel can be shaped into the desired form using various techniques like casting into molds or 3D printing.

Drying:

The hydrogel may be dried to reduce its water content, making it more stable and easier to handle.

Backing layer:

In some cases, a backing layer (e.g., non-woven fabric) is applied to the hydrogel to improve its mechanical properties and make it easier to apply to the skin.

5. Sterilization:

Ensuring sterility: If the hydrogel patch is intended for medical use, it needs to be sterilized to eliminate any potential contaminants. This can be achieved through various methods like autoclaving or gamma irradiation.

Key Considerations:

In-situ polymerization:

This method involves creating the hydrogel directly within the desired shape, often using UV curing.

Two-phase mixing:

Table No. 1: Formulating Formula for Preparation of Herbal Hydrogel Patch

Ingredient	Quantity (g or mL)	Function
Polyvinyl alcohol (PVA)	6 g	Main hydrogel backbone, film-former
Polyethylene glycol (PEG-400)	3 g	Plasticizer & humectant
Chitosan	1 g	Bioactive polymer, improves wound healing
Sodium alginate	1.5 g	Gelling agent, improves texture & stability
Sesame oil	2 ml	Emollient & occlusive
Mint extract/oil	0.3 ml	Cooling, antimicrobial
Bermuda grass juice	5 ml	Herbal active
Marigold petal extract	3 ml	Anti-inflammatory
Hibiscus leaf extract	3 ml	Conditioning & antioxidant
Yashti (Licorice root) extract	2 ml	Skin brightening & anti-inflammatory
Sadaphul flower extract	2 ml	Traditional medicinal role
Camphor	0.2 g	Cooling, antimicrobial
Amla leaf extract	3 ml	Antioxidant & vitamin C source
Mango turmeric extract	2 ml	Anti-inflammatory, healing
Purified water	q.s. to 100 mL	Solvent, hydration medium

Some hydrogels are made by combining separate aqueous and non-aqueous phases, like in the TEB gel patch example.

Micro needle patches:

These patches feature microscopic needles made of hydrogel to deliver substances through the skin.

The specific steps and materials used in hydrogel patch manufacturing can vary depending on the intended application and desired properties of the final product.

You may add preservatives (optional) like sodium benzoate if long storage is needed.

General Procedure of making Hydrogel Patch:

To make a hydrogel patch, you typically blend water-soluble polymers with additives to create a pre-gel solution, load it with active ingredients, pour it into a mold or onto a support material, and then induce gelation via chemical cross-linking or other methods like thermal treatment. The resulting hydrogel is often adhered to a support layer and allowed to age, forming a sheet that can be cut into individual patches for skincare or medical use.

1. Prepare the Polymer Solution

- Dissolve Hydrophilic Polymers: Mix water-soluble polymers, such as polyvinyl alcohol (PVA) or polyacrylic acid, with a moisturizing agent or water.
- Add Ingredients: Incorporate active skincare or pharmaceutical ingredients, fillers, and pH regulators into the mixture.

2. Induce Gelation

- Form the Hydrogel: Pour the solution into a mold or onto a non-woven fabric support.
- Cross-linking: Initiate gelation by introducing a cross-linking agent or by using thermal processes, such as heating, to form a stable 3D network.

3. Create the Final Patch

- Support Bonding: For some applications, an adhesive layer and a non-woven fabric backing are applied to the hydrogel after it has set.
- Aging & Drying: Allow the hydrogel to age at room temperature to achieve complete gelation and maturity.
- Cutting: Once aged, the hydrogel sheet is cut into individual patches of the desired size and shape.

Evaluation of Formulated Hydrogel Transdermal Patches: -

1. Physical Appearance

All the transdermal patches were visually inspected for colour, clarity, flexibility and smoothness.

2. Thickness

The thickness of the film was measured at three different points using digital thickness gauge and the average thickness was calculated. The experiment was performed in triplicate (n=3)

3. Weight Uniformity

For each formulation, three randomly selected patches were used. For weight variation test, 3 films from each batch were weighed individually and the average weight was calculated.

4. Folding Endurance

Folding endurance of the film was determined by repeatedly folding a small strip of film (2cm x 2cm) at the same place till it broke. The number of times, the film could be folded at the same place without breaking, gave the value of folding endurance.

5. Percentage Moisture Content

The prepared films were weighed individually and kept in a desiccator containing fused calcium chloride at room temperature for 24 hrs. After 24 hrs the films were reweighed and the percentage moisture content was determined by using the given formula.

$$\text{Percentage moisture content} = \frac{\text{initial weight} - \text{final weight}}{\text{final weight}} \times 100$$

6. Percentage Moisture Uptake

The weighed films were kept in a desiccator at room temperature for 24 hrs containing saturated solution of potassium chloride in order to maintain 84% RH. After 24 hrs the films were reweighed and the percentage moisture uptake was determined by using the given formula.

$$\text{Percentage Moisture Uptake} = \frac{\text{final weight} - \text{initial weight}}{\text{initial weight}} \times 100$$

7. Drug Content Uniformity

The uniformity of drug content of the transdermal film was determined, based on dry weight of drug and polymer used, by means of a UV/VIS spectrophotometer method. A specified area (2cm²) of patch was cut and dissolved in 10 ml of phosphate buffer pH 7.4. Then the solution was transferred in a volumetric flask and the volume made up to 10 ml. Appropriate dilutions were made using phosphate buffer pH 7.4, filtered and analysed for drug content at 290 nm by using UV spectrophotometer and determine the % drug content.

$$\text{Drug Content Uniformity} = \frac{\text{test absorbance}}{\text{standard absorbance}} \times 100$$

8. In-vitro Drug Permeation Study

In-vitro permeation studies were performed by using a modified Franz diffusion cell with a receptor compartment capacity of 25ml. The treated synthetic cellophane membrane was mounted between the donor and receptor compartment of the diffusion cell. The formulated patches were cut into the size of 4cm² and placed over the cellophane membrane and the receptor compartment of the diffusion cell was filled with pH 7.4 phosphate buffer.

CONCLUSION: -

Hydrogel herbal patches represent an innovative approach that integrates the advantages of hydrogel systems with the therapeutic benefits of herbal medicine. Their unique ability to maintain a moist healing environment, ensure biocompatibility, and enable controlled release of bioactive compounds makes them highly promising for wound care, skin disorders, and localized drug delivery. As research advances, these patches hold significant potential to bridge modern biomaterial technology with traditional herbal therapies, offering safe, effective, and patient-friendly treatment options.

RESULT: -

There are the wound healing propertes in herbal medicament are used in hydrogel formulation and that gel formulation converted it into the patch formulation for better patient complance. That by using solvent casting method is useful for preparing the herbal patch in that the ambi halad & amla leaf are used as main constituent for Wound healing property

REFERANCE: -

1. Indian Pharmacopia Edition 2022 Volume No.1,2,3,4 Page No. 289 ; 1112 ; 3309
2. The Big Book of Herbal Medicine by Tina Sams
3. Encyclopedia of Herbal Medicine by Andrew Chevallier
4. Analysis of carotenoid biosynthetic gene expression during marigold petal Development Department of Botany and Plant Pathology, Michigan State University, East
5. D. Bedigian and J. R. Harlan, Econ Bot., 40, 137 (1986).
6. N. M. Nayar, in N. W. Simmonds, ed., Sesame: Evolution of Crop Plants, Longman, London and New York, 1976, pp. 231–233.
7. T. Kobayashi, in A. Ashri, ed., Sesame: Status and Improvement Proceedings of Expert Consultation, The Type Classification of Cultivated Sesame Based on Genetic Char- acters, FAO Plant Production and Protection Paper 29 Rome, 1981, pp. 86–89.
8. N. M. Nayar and K. L. Mehra titled "Sesame: its uses, botany, cytogenetics, and origin" in the journal Economic Botany, Volume 24, pages 20–31
9. A. Ashri, in G. Roebblen, R. K. Downey, and A. Ashri, eds., Oil Crops of the Word, McGraw Hill, New York, 1989, p. 375.
10. J. J. Ochse, J. Soule, M. J. Dijkman, and C. Wehlburg, Tropical and Subtropical Agriculture Vol. II, Macmillan, New York, 1961, pp. 1089–1093.

11. R E S EAR CH Open Access Polyphenol composition and antioxidant potential of mint leaves Nicole Brown 1, Jenny A. John1, 2 and Fereidoon Shahid
12. Vagbhata; Ashtangahridaya; with commentaries of Sarvangasundara of Arunadatta & Ayurveda rasayana of Hemadri; annotated by Dr. Anna Moreshwar Kunte & Krishna Ramachandra Shastri Narve; edited by Pt. Hari Sadashiva Shastri Paradhakar; Chaukhamba Surabharati Prakashana; reprint 2002, pp. 430-450.
13. Sushruta; Sushruta Samhita; with Nibandha Sangraha commentary of Sri Dalhanacharya, edited by Yadavji Trikumji Acharya; Chaukhamba Surabharati Prakashana Varanasi; reprint 1994, pp. 570-580.
14. Agnivesha; Caraka samhita; with Ayurveda Dipika commentary by Chakrapanidatta edited by Vaidya Yadavaji Trikamji Acharya; chaukhamba Surabharati Prakashana Varanasi; reprint 2000, pp.324.
15. Bhavamishra; Bhavaprakasha; Vidyotini with hindi commentary by Bhishagratna Pandit Sri Brahma Sahankara Mishra; Part II; Chaukhambha Sanskrit Sansthan; 7th edition 2000, pp.510-520.
16. Sri Vaidya Sodhala; Gada Nigraha; with Vidyotini hindi commentary; by Sri Indradeva Tripathi edited by Sri Ganga Sahaya Pandeya; Part II ; Kayachikitsa Khanda; The Chowkhamba Sanskrit series office; First edition 1969; pp. 225.
17. Vagbhata; Ashtangasangraha; with Hindi commentary by Kaviraj Atrideva Gupta; Krishnadasa Academy; reprint 1993, pp. 430-450.
18. Sharanghadhara; Sharanghadhara Samhita; English translation By Prof.K.R.Srikanthmurthy Chaukhambha Orientalia Varanasi, Second edition 1995, pp.280-290.
19. Sharma PV. Ayurveda ka VaijnanikaItihasa Abridged edition. Varanasi; Chaukhambha orientalia. 4th edition 2001, p-13.
20. Sofowora A. Medicinal Plants and Traditional in Africa. Chichester John Wiley and Sons, New York. 1993;p-97-145.
21. PKk Nair. Glimpses in plant research. V-4, 1979, page no.160.
22. Vickers A, Zollman C. ABC of complementary medicine: herbal medicine.
23. handel HS, Pathak A, Tailang M. Polyherbal formulations for anti-diabetic therapy. Int J Pharm Pharm Sci. 2011;3(3):226-8.
24. Bajpai VK, Agrawal P. Studies on Phytochemicals, Antioxidant, Free Radical Scavenging and Lipid Peroxidation Inhibitory effects of Trachyspermum ammi seeds. Indian Journal of Pharmaceutical Education and Research. 2015;49(1):58-65.
25. Kokane, D.; More, R.; Kale, M.; Nehete, M.; Mehendale, P.; Gadgoli, C. Evaluation Of Wound Healing Activity Of Root Of Mimosa Pudica. Journal of Ethnopharmacology 2009, 124, 311-315.
26. Epstein, F.; Singer, A.; Clark, R. Cutaneous Wound Healing. New England Journal of Medicine1999, 341, 738-746.
27. Broughton, G.; Janis, J.; Attinger, C. The Basic Science of Wound Healing. Plastic and Reconstructive Surgery 2006, 117, 12
28. Braiman-Wiksman, L.; Solomonik, I.; Spira, R.; Tennenbaum, T. Novel Insights into Wound Healing Sequence of Events. Toxicologic Pathology 2007, 35, 767-779.
29. Dreifke, M.; Jayasuriya, A.; Jayasuriya, A. Current Wound Healing Procedures and Potential Care. Materials Science and Engineering: C 2015, 48, 651-662