

Evaluation of Antimicrobial, Anti-Inflammatory and Wound Healing Potentiality of Various Indian Small Herbs: A Meta Analysis

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ABSTRACT

The immune system has the ability to provoke inflammation in response to a wide variety of different triggers. Toxic chemicals, infectious diseases, radiation, and cells that have been harmed are some examples of these stimuli. It removes the detrimental stimuli and at the same time initiates the healing process, which is a win-win situation. As a result, the protective reaction of inflammation is essential for ensuring that the body continues to function properly. The majority of the time, cellular and molecular activities and interactions work together to successfully minimise the risk of experiencing damage or infection during acute inflammatory reactions. This is because these activities and interactions are coordinated to function together. This review article was prepared utilising materials written in English, and it has been published in time intervals of 15 years beginning in 1995 and continuing all the way up until the current day. Both systematic reviews and randomised controlled trials (RCTs), which are considered to be the two most reliable types of research, were included in the collection of publications that were pertinent to the goal that we set for ourselves. The first two approaches are the only ones that should be prioritised above the others. Studies with an open label and studies with cohorts are not as essential as those with a case-control design, which are called preclinical trials.

Keywords- Immune system, inflammatory diseases, healing, anti microbial.

I. INTRODUCTION

Inflammation is a response that is elicited by the immune system in response to many stimuli. Some examples of these stimuli are toxic substances, infections, damaged cells, and radiation. It gets rid of the harmful stimuli and kickstarts the healing process at the same time.¹⁻⁵ Therefore, the protective response of

inflammation is necessary for maintaining overall health. During acute inflammatory responses, the majority of the time, cellular and molecular activities and interactions work together to effectively lower the danger of suffering damage or infection. As a consequence of these processes, the homeostasis of the tissues is brought back to normal, and the acute inflammation is completely wiped out. On the other

hand, acute inflammation that is left untreated can, if it is not effectively managed, result in a wide variety of chronic inflammatory illnesses.⁶ An infection or injury can cause redness and swelling, as well as heat and discomfort, and impaired tissue function at a cellular level. Inflammatory mediators are produced in greater amounts when the microcirculatory system is irritated, as well as leukocyte recruitment and accumulation. Inflammation can be triggered by a variety of stimuli, including both infectious and noninfectious microorganisms.⁷⁻¹⁵ When you use this strategy, you'll see an overall improvement in your health right away. Swelling (tumour), heat (calor), redness (rubor), pain (dolor), and loss of function are some of the most typical indicators of inflammation (functio laesa). As the healing process progresses, there are three types of inflammation: acute inflammation, which occurs immediately after an injury and lasts a few days; chronic inflammation, which can last for months or even years if acute inflammation does not resolve; and subacute inflammation, which occurs during the transition from acute to chronic. The body produces cytokines, acute-phase proteins, and chemokines as a symptom of acute inflammation. Acute inflammation is further evidenced by the fluctuating levels of neutrophils and macrophages in the blood. In the early stages of a disease, these cells, which are part of the body's natural defence system, can cause inflammation.¹⁶ T lymphocytes and plasma cells will be drawn to the location if the inflammation persists for six weeks. As a result, acute inflammation will proceed from a subacute to a chronic stage. The tissues will be harmed and fibrosis will develop if this continues for an extended period of time. Acute and long-term inflammation is caused by macrophages and monocytes, two types of cells. "Acute inflammation" will be the primary subject of this paper.¹⁷

II. MATERIAL & METHOD

The data for this study came from a variety of sources, including PubMed, ScienceDirect, and Google Scholar. When we were searching for information in the database, we used the terms "anti-inflammatory," "plant," "herb," and "herbal medicine." This review article was compiled using sources written in English, and it was published in time intervals of 15 years beginning in 1995 and continuing up until the present day. The collection of papers that were relevant to our objective included both systematic reviews and randomised controlled trials (RCTs), which were the top two kinds of evidence. Only the first two methods are more essential than the rest. Case-control studies and preclinical trials are more important than open-label studies and cohort studies. The inclusion of RCT studies, for instance, is a clear sign that this topic has been given top importance in the literature due to the high scholarly worth it possesses. This can be deduced from the fact that this topic has received a lot of attention.

NEEM (Azadirachta indica):



Fig 1: Azadirachta indica

Antimicrobial resistance has become a major problem in recent years as a direct result of the extensive use of antibiotics to treat infections caused by the pathogenic bacteria *V. vulnificus*. The potential of NE to inhibit the growth of the dangerous bacteria *V. vulnificus* was investigated, and the minimal effective concentration (MIC) of NE that was shown to be effective in doing so was determined.¹⁸ When the NE was tested in the laboratory against the bacterium *V. vulnificus*, it was discovered to have antibacterial activity at a minimum inhibitory concentration (MIC) of 150 µg/mL. Well-diffusion and sterile-disc testing were two of the methods that were utilised in the process of determining antimicrobial susceptibility. At a concentration of 150 µg/mL, an inhibition zone of 15.3 x 0.5 mm was observed surrounding the NE; however, this dose produced no inhibition zone in the control well. A comparison was made between the antibiotic disc loaded with NE and the commercially available antibiotic disc. The inhibition zone of the NE was measured at 21.6±1.5 mm,¹⁹ while the inhibition zone of the tetracycline that is readily accessible on the market was measured at 32.3±1.5 mm. Even though the minimum inhibitory concentration for neem extracts was 6 mg/mL, it was demonstrated that NE at a concentration of 150 µg/mL²⁰ was effective against the pathogenic bacterium *V. vulnificus*. In the fight against *Aeromonas salmonicida*, *Klebsiella pneumoniae*, *Vibrio speciosus*, and *Pseudomonas alginogenica*, previous research has shown that the NE is more effective as an antibacterial agent than neem oil is. The key explanation for this was the extremely small droplet size of the NE, which made it significantly simpler for it to enter the bacteria than it was for the neem oil. It has been found that bacteria that have a thick layer of lipids are more resistant to the effects of antimicrobial medications. When compared to the bulk material that was used in the manufacture, the NE that was created using the surfactant was able to break through lipid barriers and increase the sensitivity of bacterial cells.²¹

Chrysopogon zizanioides:



Fig 2: Chrysopogon zizanioides

In order to study the facultative anaerobes, an altered version of the broth microdilution method was utilised. The wells of a microtiter plate with 48 wells were each filled with 100 μ l of the optimal culture medium (*S. aureus*, *S. epidermidis*, or *S. pyogenes* containing about 1×10^6 CFU/mL), as well as 100 μ l of freshly prepared *C. zizanioides* emulsified lotion at the optimum high-low buffer concentration. After thoroughly combining the broth, formulation, and inoculum contained in each well, one hundred litres were transferred to the following well, which was then filled with sterile sodium chloride at a concentration of 0.9 percent (NaCl). After performing serial dilutions on each sample, the microtitre plates were then put through an incubation process that was tailored to meet the optimal incubation needs of the pathogen. At intervals of 0, 3, 6, and 24 hours, samples of 50 μ L were taken from the wells. These samples were then placed on agar plates that had been prepared in advance (Tryptone Soya agar for *S. aureus* and *S. epidermidis*, and Haemophilus agar for *S. pyogenes*), and they were incubated according to the conditions that were specified for each agar strain.²³⁻²⁵

Vetiveria zizanioides:



Fig 3: Vetiveria zizanioides

The minimum inhibitory concentrations (MICs) of five unique samples of vetiver essential oil were determined by testing them against Gram-positive and Gram-negative bacteria (minimum inhibitory concentrations). It has been demonstrated that CXE oil is ineffective against bacteria such as *Staphylococcus aureus* (MIC = 78 μ g/mL), *Bacillus subtilis* (MIC = 345.6 μ g/mL), *Escherichia coli* (MIC = 321.8 μ g/mL), and *Pseudomonas aeruginosa* (MIC = 2800 μ g/mL). The Gram-positive bacterium *Staphylococcus aureus*, which is the same as CXE oil, showed only a modest amount of activity against SFE oil, although it showed a low level of activity against *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Escherichia coli*. The essential oil that was extracted from vetiver root using high-pressure distillation was shown to have a moderate antibacterial effect on the following bacteria: *Staphylococcus aureus* (MIC = 39 μ g/mL), *Bacillus subtilis* (MIC = 324.3 μ g/mL), *Pseudomonas aeruginosa*, and *Escherichia coli* (MIC = 346.7 μ g/mL). LFO (light fraction oil) from IVD exhibited clear antibacterial capability (MIC = 78 μ g/mL) against *Staphylococcus aureus*, but HFO had the opposite effect (MIC = 156 μ g/mL). *Staphylococcus aureus* is a Gram-positive pathogen. The findings of the research indicate that conventional and traditional methods are equally successful in combating Gram-positive bacteria, notably *Staphylococcus aureus*.²⁷⁻³⁰

Lannea welwitschii & Justicia flava



Fig 4: Lannea welwitschia



Fig 5: Justicia flava

Antibacterial effectiveness of methanol leaf extracts (JFL and LWL) and reference medicines were evaluated using the method used by Agyare et al (chloramphenicol and clotrimazole). The extracts were tested on Sabouraud agar and nutritional agar (both made by Oxoid Limited in the UK) to see if they have antibacterial and antifungal properties. Plates of nutritional agar and sabouraud agar were seeded with 10⁶ cfu/mL of 100 micro micro organisms from the test organisms, which included *Staphylococcus aureus* ATCC 25923, *Bacillus subtilis* NCTC 10073, *Escherichia coli* ATCC 25922,³⁴ and a clinical strain of *Candida albicans*. Well, An incubation period of 24 hours at 37 degrees Celsius and three days at 30 degrees Celsius was used to analyse the zones of growth inhibition afterward (for the fungus *C. albicans*). It was not possible to detect any antibacterial activity when DMSO was employed alone as a negative control, according to the researchers. *C. albicans* and bacterial test organisms were cultured at 37 degrees Celsius for 24 hours with a little piece of seeded agar without growth streaked on a Petri plate and determined to be at the minimum bactericidal concentration (MBC).³⁶

Rubia cordifolia:



Fig 6: *Rubia cordifolia*

Pour plate analysis was utilised in order to evaluate the antibacterial activity of the manufactured ZnO-MJE-NPs in relation to the organisms that were put to the test (*S. Aureus* and *E. Coli*). The experiment made use of agar media that had been sterilised. The distribution of the test samples was done with water that had been pasteurised. After being melted and transferred to Petri plates, the sterile nutrient agar medium was then mixed with the bacteria and allowed to harden without any agitation. After using a sterile borer to create a well that was 10 millimetres in diameter, one millilitre of the drug that contained between 20-320 µg/mL of MJE was introduced. After that, the Petri plates were put away for a few hours, and then they were placed inside an incubator for a period of twenty-four hours. Throughout the course of the experiment, ZOI was analysed on a millimeter-by-millimeter scale. This was carried out three times (mm).

Jasminum auriculatum:



Fig 7: *Jasminum auriculatum*

Degrading the bacterial membrane and inhibiting the production of cell walls and nucleic acid are the two primary modes of action that are utilised by the majority of antibacterial drugs. Bacterial strains are able to endure and develop antibiotic resistance by a wide number of distinct processes. These processes can be broken down into subcategories. Antibiotic resistance can develop from a number of different mechanisms, such as changes to bacterial target structures, mutations in target molecules, the overexpression of efflux pumps, the formation of biofilms, the degradation or modification of antibiotics, enzyme-mediated destruction,³⁶ and so on. According to the methods outlined above, bacteria are able to withstand the selective pressure exerted by antibiotics. Numerous bacterial enzymes have the ability to degrade antibiotics by hydrolyzing them, transferring their functional groups to other molecules, and changing their structures, all of which result in a loss of effectiveness. The -lactam class of antibiotics can typically be destroyed through hydrolysis, which is the most common approach. When antimicrobial agents are flushed out of the cell, the concentration of those agents within the cell decreases, rendering those antimicrobial agents ineffective.³⁷ This is the principal mechanism by which bacteria acquire resistance. Alterations to chromosomal genes and changes in the genomes of bacteria could both play a role in the evolution of these defence systems. Plasmids that contain resistance genes may also be responsible for conferring antimicrobial resistance in bacteria. The amount of bioactivity that a plant's active ingredients contain is directly proportional to the amount of activity that the plant displays.³⁸ It is believed that the principal effects of plant bioactive substances (PBS), which have

not been researched in great detail, are a decrease in the potential of the cell membrane and a decrease in the amount of ATP that is produced. Plasmodium bifidum (PBS) causes cellular membranes to become permeable, which ultimately leads to the death of bacteria.⁴⁴⁻⁴⁷ PBS also chelates metal ions and disrupts the action of membrane-bound ATPase, all of which contribute to the death of bacteria. PBS has the capacity to influence the pathways that bacteria use to produce resistance in a wide variety of different ways. Inhibitors of drug-inactivating enzymes and inhibitors of efflux pump over-expression both play critical roles in their operation. In addition to this, they inhibit the production of proteins and DNA, and they serve as an anti-biofilm agent. In addition to carvacrol, other compounds such as eugenol, thymol, and catechins have been found to cause ATP depletion via disrupting the membrane structure. This link was shown.⁴⁸ It is also capable of interfering with membrane permeability and disrupting the cell membrane, which finally leads in cell death in resistant bacteria. Tea tree oil is made up of monoterpenes and terpenes, sesquiterpenes, 1,8-cineol and alpha-terpineol, and terpinen-4-ol. Tea tree oil includes monoterpenes, which have been shown to provide a variety of health benefits (Staphylococcus aureus, Escherichia coli, and Candida albicans).⁴⁸

The numerous phytoconstituents that can be found in Jasminum spp. are briefly discussed in the following paragraphs. There are alkaloids, phenolics, saponins, steroid, tannin, and terpenoids found in the root bark of Jasminum angustifolium. Jasminum angustifolium leaves also include alkaloids, phenolics, saponins, sterols, tannins, and terpenoids. Both the Jasmine angustifolium and the Jasmine angustifolium subspecies sessiliflorum have been reported to contain anthraquinones. In addition to alkaloids (quinones), flavonoids, phenols, saponins, and terpenoids, the plant's flowers and leaves contain a variety of other chemical compounds.⁴⁹

The flower of the Jasminum auriculatum plant has significant quantities of flavonoids, phenolics, and terpenoids. Alkaloids, essential oil, flavonoids, glycosides, phenolic acid (salicylic acid), sterols, and tannins can all be found in the blooms of this plant. In addition to flavonoids, alkaloids, glycosides, azoricin and sambacin, as well as other iridoid glucosides, the leaves of Jasminum azoricum contain other iridoid compounds.⁵⁰ Other iridoid glucosides are also found in these leaves (such as rutoside and quercetin). Sesquiterpenoids were found in Jasminum brevilibum leaf samples (jatamansone).⁵¹ There are a wide range of chemical substances in Jasminum fluminense's leaves and flowers, including as alkaloids, flavonoids, glycosides, phenols, saponins, and triterpenes (squalene). Fragranced Jasmine grandiflorum is noted for its high content of flavonoid (rutoside), monoterpene (geraniol, isothiocyanates), sesquiterpene alcohol (eugenol), flavonoids (cresol), and other phytochemicals (eugenol,

geraniol, isothiocyanates, secoiridoids). Alkaloids and flavonoids have been found in the leaves of Jasminum nervosum.⁵²

It is found in the leaves of Jasminum officinale, which are high in polyphenols (phenols, phenylethanoids, flavonoids, and secoiridoid glycosides), as well as phenolics, phenylethanoids, and flavonoids. It is used to treat a variety of conditions, including inflammation and cancer (sulfurein).⁵³ In addition, sesquiterpenoids can be detected in the stem of this plant. Alkaloids, phenols, quinines, saponins, and terpenoids have been found in both the leaves and the flowers of the Jasminum polyanthum plant. The blooms and stems of the Jasminum syringifolium plant contain a variety of chemicals, including all of those listed below as well as others.

Curcuma longa L.



Fig 8: *Curcuma longa* L.

Methicillin-resistant Staphylococcus aureus, or MRSA, is becoming a more common infection in hospitals and communities around the world. As a result, new treatments are needed for MRSA infections. Curcuma longa L. (*C. longa*) extracts in ethyl acetate, methanol, and water were tested against MRSA in this study.⁵⁴⁻⁵⁷ An ethyl ester extract (EAE) of *C. longa* was shown to have better antibacterial activity than either a methanol or water extract. Beta-lactam antibiotic activity was restored when ethyl acetate, a more active extract, was used, and MRSA penetration in human mucosal fibroblasts was altered. To see if the ethyl acetate extract of *C. longa* reduced the MICs of ampicillin and oxacillin against MRSA, researchers performed a checkerboard test. The inclusion of *C. longa* extract reduced the amount of intracellular MRSA invasion significantly compared to the control group during the bacterial invasion test. *C. longa* extract has both antibacterial activity and the ability to restore the efficacy of beta-lactams against MRSA, as well as the ability to prevent MRSA invasion of HMFs, according to this study's findings. Preventing MRSA from spreading requires both of these skills.^{58,59}

B. aristata



Fig 9: *B. aristata*

Following intraplantar injections of Carragenan into the right hind paw of rats, edoema was noticed in the animals. When compared to the control group, the amount of volume in the paws was dramatically decreased by the *B. aristata* extract.^{60,61} When compared to regular gel, transferosomal gel had a 33.5 percent higher rate of success in inhibiting edoema (optimized batch-55.76 percent). The major irritation scores of both gel formulations are both 0.4, which indicates that the preparations are safe for topical use and cause just a minimum amount of irritation. We studied the anti-hyperlipidemic action of *Berberis aristata*, *Silybum marianum*, and monacolins K and KA, and we observed that LDL-C was lowered by around 31.6 percent when compared to the baseline value.⁶² In earlier clinical tests, the combination of *Berberis arista* and *Silybum marianum* as a nutraceutical resulted in a reduction of LDL cholesterol of about 24 percent, which is comparable to the findings presented here. When we previously studied a nutraceutical combination of monacolins and Coenzyme-Q10, there were no effects on HDL-C or Tg; however, there was a reduction of 22 percent in both total cholesterol and LDL-C. This indicates that the improvement in LDL-C might be attributed to monacolins K and KA, while the reduction in Tg could be attributed to *Berberis aristata* and *Silybum marianum*.⁶³

Oenothera biennis



Fig 10: *Oenothera biennis*

One of the most studied members of the Onagraceae family is the evening primrose, *Oenothera biennis* L. (OB).⁶⁴ This plant is also known as the evening primrose. Oils extracted from seeds, known as "aerial oils," can have a wide range of medicinal effects, including anti-inflammatory properties. Study objectives were to analyse the phytochemical content and biological activity of the hydroalcoholic extract of the OB melanoma cell line, as well as to determine whether the extract was able to prevent the growth of bacteria, halt cell proliferation, and induce senescence. Gallic acid, coumaric acid, ferulic acid, rosmarinic acid, and epicatechin were determined to be the most common polyphenols and flavonoids. 625.578 µgGAE/mL phenolic content and 7359.87 µmolTrolox/g extract antioxidant activity were determined in the extract.⁶⁴ That is, it appears to have a mild impact on the bacteriostatic capacity of the bacteria that are being examined in this study Those belonging to the *Candida* and *Staphylococcus* species were the only microbes that could destroy it. The A375 human melanoma cell line demonstrated a substantial antiproliferative and proapoptotic effect against the extract at 60 µg/mL, the maximum dose tested. As the concentration of OB extract in the A375 cells increased, their ability to migrate decreased. At the highest concentrations tested, the OB extract inhibited the angiogenic process and the mitochondrial activity in vitro,⁶⁵ preventing the formation of a compact tumour. An anti-inflammatory effect was observed in the experimental animal model of ear irritation that was treated with the extract of OB. Olive leaf extract is known as OB.^{66,67}

Harpagophytum procumbens



Fig 11: *Harpagophytum procumbens*

A great number of bacteria have developed resistance to various medications. As a result, research into new antiseptics and antibacterial agents is being conducted to treat skin infections, which are becoming an increasingly important area.⁶⁸ In order to determine whether or whether these six plant extracts and their

extracted components have antibacterial characteristics, they were tested against bacteria and yeasts that are significant to dermatology. Dry extracts of *Usnea barbata*, *Rosmarinus officinalis*, and *Salvia officinalis* have also been studied and tested for their medicinal properties (supercritical carbon dioxide [CO₂] extracts).⁶⁹ Further research focused on the chemical compositions of a number of other plant constituents, such as usnic and carnolic acids, as well as alpha- and beta-ursolic acids, boswellic acid and gentiopicoside (a derivative of alpha-ursolic acid). Chemicals and extracts were evaluated against 29 different types of aerobic and anaerobic bacteria and yeast using the agar dilution method. The extracts and compounds tested were found

to be effective against all of the tested species. In anaerobic bacteria, both the *U. barbata*-extract and usnic acid were found to be the most potent chemicals. An inhibitory effect on the growth of *S. aureus* (including methicillin-resistant strains; MRSA), *Propionibacterium acnes*, and *Corynebacterium* species has been proven by the *Usnea* CO₂-extract. The *Usnea* extract also reduced the growth of a yeast known as *Malassezia furfur*, which can change its appearance. Apart from *Rosmarinus*, *Salvia*, *Boswellia*, and *Harpagophytum* extracts,⁷⁰ *Usnea* extract has been proven to be effective against many types of bacteria. *Acne vulgaris* and seborrheic eczema can be treated with plant extracts that have antibacterial properties.

Table 1: Chemical Constituents Present in Indian herbs shows Antimicrobial effects

Plant name	Family	Chemical Constituents	References
Neem	Meliaceae	azadirachtin and the others are nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinat, gedunin, salannin, and quercetin	51
<i>Chrysopogon zizanioides</i> :	Poaceae	Cycloisolongifolene, isodene. β -patchoulene	52
<i>Vetiveria zizanioides</i> :	Poaceae	Cycloisolongifolene, isodene. β -patchoulene	53,54
<i>Lannea welwitschii</i>	Anacardiaceae	Dihydroxycyclohexenones, cyclohexene triols	55
<i>Rubia cordifolia</i>	Rubiaceae	saponins, tannins, proteins, and glycosides	56
<i>Harpagophytum procumbens</i>	Pedaliaceae	Myo-inositol (monosaccharides), galactose, glucose, and raffinose (46 percent), as well as sucrose (oligosaccharides)	57

Table 2: Pharmacological Activity of Indian herbs

Plant name	Parts of Plants	Pharmacological Activity	References
Neem	Stem	There are numerous qualities that make it an excellent immunomodulator, such as its ability to reduce inflammation and inflammation-related conditions including hyperglycemia.	60
	Root		
	Fruit		
	Leaves		
	Seed		
<i>Chrysopogon zizanioides</i> :	Stem	Pain, Anti- acnes , antibacterial, antiviral, antioxidant	70
	Root		
	Fruit		
	Leaves		
	Seed		
<i>Vetiveria zizanioides</i> :	Stem	Pain, Anti- acnes , antibacterial, antiviral, antioxidant	71,72
	Root		
	Fruit		
	Leaves		
<i>Lannea welwitschii</i>	Stem	Diarrhoea, dysentery, urethral discharge, and haemorrhoids are all	74
	Root		

	Fruit	common female diseases. To cure wounds and snakebites, you can use the bark as a pulp or a powder, according on your needs.	
	Leaves		
<i>uRubia cordifolia</i>	Stem	Analgesic and wound healing properties. Antibacterial and antioxidant properties. Anticancer and anti-inflammatory properties. Antiplatelet activating factor.	75,76
	Root		
	Fruit		
	Leaves		
Harpagophytum procumbens	Stem	inflammatory disorders	
	Root		
	Fruit		
	Leaves		
	Seed		

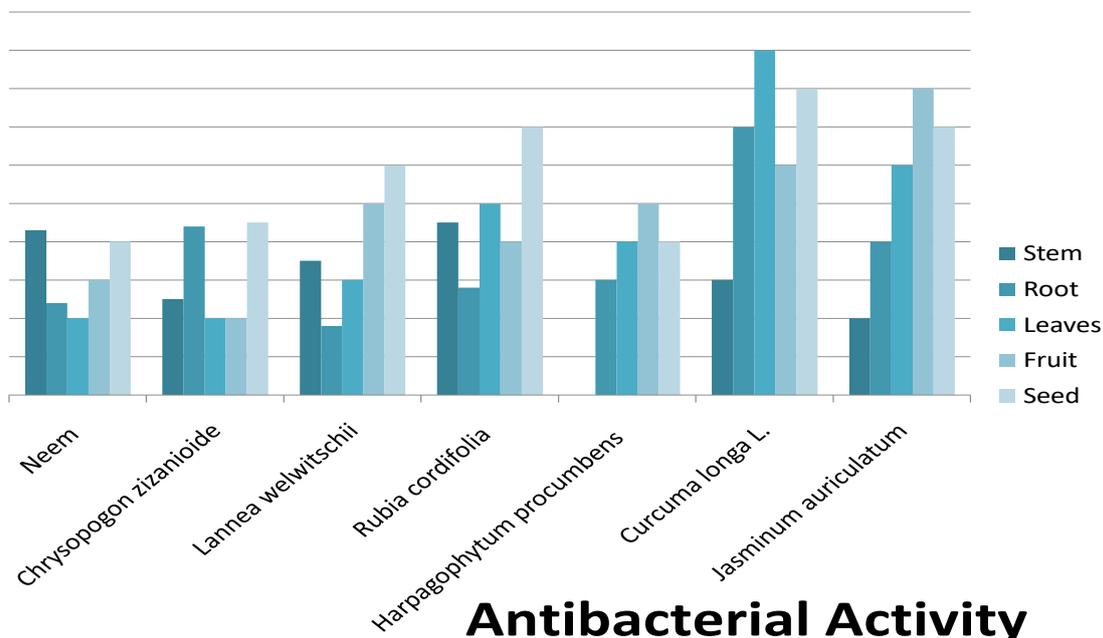


Fig. 12: Graph shows antibacterial activity of various herbs

III. CONCLUSION

Infections of the skin and wounds are among the most prevalent health concerns that individuals of all ages might experience. In the treatment of skin and wound infections, medicinal herbs and the components of those plants are frequently utilised in addition to the conventional pharmacotherapy. In today's world, the effects of natural products derived from plants and the mechanisms that underlie their activity have been the subject of experimental research, with the findings indicating that these products have a complex effect that is beneficial in the treatment of skin and wound infections. The ultimate effects of herbal therapeutic goods continue to be complicated due to the numerous elements found in these items. Numerous plant extracts have qualities that aid in the healing of wounds in addition to their antibacterial and anti-inflammatory

activities. Traditional herbal medical medicines, which have already established appropriate safety evidence and probable efficacy, are what the European Medicines Agency (EMA) advises for skin problems. This article provides a comprehensive assessment of the biologic activities of many suggested herbal medications and their ingredients, with a particular emphasis on the antibacterial properties of these substances.

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