

REVIEW ARTICLE

Prospective Influence of Phytotherapy on Resistant Bacterial Tonsillitis

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Abstract

The emergence and evolution of superbugs is among the greatest challenges to public health worldwide recently. Bacterial resistance to antibiotics considered as one of greatest hits of this century. There are different antibiotic resistant strains that range for infection from mild to severe cases and tonsillitis is one among of many bacterial diseases that have high incidence globally. Half of tonsillitis cases are bacterial and those mainly caused by group-A beta-hemolytic *streptococci* (GABHS) bacteria which had developed its resistance against commonly used antibiotics, mainly penicillin and macrolids. Currently, however, there are considerable attempts to tackle the issue despite they are still far away from promised settlement. Focusing on testing and evaluating of herbal therapies will be of great value in finding of potent alternative medicine to face resistant bacterial infections and to provide sufficient therapeutic agent to disband the problem. Hence the necessity to develop novel therapeutics to replace conventional antibiotics will likely play a key role to fix the issue. This article concentrate on review of ineffective antibiotic therapy including some of its impacts and describes possibility to use *Saussurea lappa* (*S. Lappa*) plant as an effective herbal plant to treat resistant bacterial acute tonsillitis cases.

Keywords: Bacterial resistance, β -hemolytic *streptococci* bacteria, Broad spectrum activity, *Saussurea lappa*, Tonsillitis.

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INTRODUCTION

Thousands years ago, the human being exposed to many infectious diseases ranged from amiable to lethal cases. He struggled to face, cure such diseases and to find specific treatments. Bacterial infections play significant role among other types of infectious diseases. Bacterial infections are one of the most dangerous infections that threaten the existence and continuity of life. Despite the discovery and manufacturing of effective antibiotics to tackle this menace, bacteria have digged its way to live and develop resistance against these treatments and transformed into new mutant resistant strains. Tonsillitis is one of the critical bacterial infections that hits globally, it affects throat and can be viral or bacterial¹. Thirty percent of cases caused by group-A beta-hemolytic *streptococci* (GABHS) bacteria ². Generally, treatment depends on causative agent and course of disease accordingly, because that tonsillitis may occur in the form of chronic or acute condition. However acute bacterial cases routinely treated by broad spectrum antibiotics and symptomatic therapy (by non-steroidal anti-inflammatory drugs [NSAIDs]), a rationale that deduce we need a combination of multiple treatments to get rid of tonsillitis.

Long time ago, antibiotics were used to treat many different bacterial infections and their discovery printed a foot on a map of our medicine. Eventually, with their uncontrolled widespread usage, the bacteria carpe diem and the condition leads to developed drug resistance to these organisms³. Currently, our health vulnerable to hazards of antibiotics resistance. First of all, the end fate of failure of treatment. Then its peripheral impacts, antibiotic resistance increases healthcare costs due to ineffective treatment courses, causes people to stay in hospital longer, results in treatment failures and sometimes death⁴. Therefore, rigorous research activities are being carried out around the globe to develop alternative methods for treatment of infectious diseases caused by multi-drug resistant (MDR) bacteria, these include using of bacteriophages, phage lytic enzymes, bacteriocins, antimicrobial peptides or herbal medicines. Traditional herbal medicine by medicinal herbs seems to be a good option for this problem.

From early human life, traditional herbal

medicine based on medicinal plants application according to experience and practice through trial and error method⁵. Medicinal plants used today were known to people of ancient cultures all over the world long time ago and their application continuous to grow due to experienced potency without undesired effects. For instance, due to their anti-inflammatory and anti-septic properties they were used to treat many inflammations⁶. *Saussurea lappa* (*S. lappa*) is one of the reported plants which used to treat many inflammatory conditions like sickness of women after delivery⁷. This article will focus on treatment of resistance problem in tonsillitis cases and possibility to apply *S. lappa* for its treatment instead of using conventional antibiotics.

LITERATURE REVIEW

Our health is endangered by arising of superbugs, those bacteria which developed a powerful resistance to utmost already developed antibiotics. Many reports from dependable foundations (e.g. World Health Organization [WHO] and Centers of Disease Control and prevention [CDC]) revealed the outbreak of problem and disclosed predictable riskiness that threaten our life⁸. Review of related previous literature uncovers the horrible image of bacterial resistance issue and the importance of herbal medicine to stand up against the problem. For that this paper centralized upon finding proper herbal remedy to overcome on resistant bacteria at least in case of tonsillitis infection.

Background of Tonsillitis

Tonsillitis is defined as inflammation of palatine tonsils, which is infection and inflammation of tonsils (glandular tissue on either side of the back of throat)². Our tonsils are considered as one of the important part in our primary immune system¹². Their inflammation is a complex pathophysiological defense reaction of vascular tissues in a response to harmful stimuli that can be distinguished by certain symptoms and signs⁹. Its symptoms involve sore throat with difficulty swallowing (dysphagia), hoarse or muffled voice, localized pain especially with swallowing process, fever, loss of appetite, general unwell, drooling, swollen associated lymph nodes, adenopathies, glossitis and palatine petechiae may be included, in advanced cases, abdominal pain

and vomiting may be reported². Signs embrace congestion of pharyngeal mucosa, sometimes with or without purulent exudates, ulcers, blisters and swollen erythematic tonsils covered by white or yellow pustules².

As many inflammatory conditions, tonsillitis appears as acute, chronic or recurrent condition. Recurrent attacks characterized by hypertrophic tonsils' glandular tissue followed by difficulty in swallowing and breathing, persistent pain and general malaise, all of these in turn affect daily life from many aspects. Acute condition may progress to recurrent one that needed to be treated surgically by tonsillectomy¹⁰.

Acute tonsillitis may occur due to viral or bacterial infection and just slight diagnostic differences between them can be noticed by clinical observation, the matter that necessitate clinicians to apply cultural swabs for lab diagnostics. Many reports show that there is misdiagnosis of tonsil cancer too, in which reported cases were diagnosed by general practitioners as tonsillitis cases then after long time of resistance of disease to treatment by antibiotics they suggested by specialists they are cancer cases. A study by Dubai et al., (2012) aimed to reveal importance of education of related knowledge among students, the matter that this condition needs intensive knowledge and experience¹¹.

Bacterial etiology characterized by pus formation, and most of cases gets infectious bacteria via mouth, while viral cases characterized by hemorrhagic oozing and infectious virus directed from nose route. Furthermore, viral cases of tonsillitis have short attacks and mostly resolve spontaneously. Tonsillitis causative agents include *Streptococcus pyogenes*, *Staphylococcus aureus*, *Corynebacterium diphtheria*, Candidiasis, Vincent angina, Adenovirus, Adeno-associated viruses and Corona virus⁷⁷. Fifty percent of cases are bacterial. The most common causative bacterial agent is β -haemolytic *Streptococci* bacteria group A (GABHS). Its infection known clinically as follicular tonsillitis and famously by strep throat. Chronic tonsillitis differs from acute condition by persistent recurrent attacks of acute one and tonsils beside throat tissue severely affected and become as a site of infective organisms.

In general, tonsillitis treatment depends on cause and course of the disease with some

common regulations such as all cases should be proceeded by throat swab for laboratory investigation, with consideration of home care and rest for both acute and chronic cases, avoiding contact with risk people, eating soft cold foods, fluids and soups, gargling with salted water and using throat lozenges and mouth washes like glycerol-thymol gargle that has a value to act as a local antiseptic, release the pain and prevent sepsis¹.

In one hand, first drugs of choice to treat acute bacterial tonsillitis cases are broad spectrum antibiotics such as Penicillin V (benzyl or phenoxymethyl penicillin). It is preferred to use with cases of resistance to other antibiotics. Some antibiotics can aggravate tonsillitis condition like Ampicillin, which causes rash sensitivity especially with infectious mononucleosis patients¹³. Other treatments include NSAID mainly Paracetamol to reduce fever and to relief inflammation.

On the other hand, treatment of chronic cases mainly surgically by tonsillectomy. It is recommended for persistent acute and chronic tonsillitis, and partially indicated for recurrent acute tonsillitis. Urgent absolute indication of tonsillectomy in cases of sleep apnea, respiratory obstruction and in suspicion of malignancy, and relatively indicated for chronic and recurrent acute cases, quinsy and for diphtheria carriers¹⁴.

Not tonsillitis alone! Many respiratory tract infections constitute major health issue such as flu, bronchitis, influenza and pneumonia which their common symptoms and signs are somehow similar to tonsillitis with slight differences. Physicians and scientists are on challenge to confer safe potent medicines for such cases^{15,16,78}. Many of last mentioned cases were treated by antibiotics, which indicate the extent of their usage in treatment of many medical cases.

According to PubMed study related to this article, it revealed that acute upper respiratory tract infections (AURTI) was the most condition for bacterial infectious diseases to prescribe antibiotics, this was by percentage of 49.2% in Malaysia in 2016. Furthermore, the study disclosed that AURTI were among the top four indications in a given study. This study revealed two findings, firstly, people were mostly undergone an infection of upper respiratory tract among other infectious diseases. Secondly, doctors had prescribed

antibiotics at high rates. Both matters lead to deduction of importance of AURTI especially tonsillitis, and the urgent need to substitute antibiotics by novel treatment¹⁶.

Bacterial Resistance to Antibiotics

Resistant tonsillitis or rather microbial resistance to antibiotic treatments considered as one of problem based learning (PBL) in which the medical researchers need how to deal with clinical problem and how to extract the solution upon related training, this is accomplished within three phases: Problem analysis, Self-directed study and Synthesis and application of newly acquired information¹⁷.

Development and mass production of antibiotics to treat various bacterial infections was one of the brightest scientific efforts in the last century. They gained their importance and reliability from their effectiveness⁷⁸. Over the past sixty years, clinicians have been depending on them to treat bacterial infections. As a result of their frequent and uncontrolled use, bacteria have developed resistance against them and thus transformed those drugs to less effective agents^{3,19}. Recently, those miracle drugs have lost their importance as most of the pathogenic bacteria have become resistant to most or all available antibiotics^{20,21}.

Although trials of developing of new classes of antibiotics have continued with time, but it has declined in recent few years. Since 1987, no new classes of antibiotics have been developed even with the help of modern biotechnology²². The main problem was that pharmaceutical companies focused only on production of antibiotics from previous known classes^{23,24}, at the time that antibiotic resistance problem continued to grow in the absence of real solution.

Prolonged usage of antibiotics encourages bacteria to develop "supergenes". These are mutations that give ability to bacteria to resist almost all available antibiotics²³. However using the modern biotechnology tools, many experiments suggested the presence of antibiotic resistant genes^{26,27,28}. In turn these bacteria become superbugs that are resistant to all or most available antibiotics.

Generally, with the possibilities of using of many biomedicine practical fields, such as biotechnology for sequencing and cloning,

scientists could understand many of these pathogenicity mechanisms at a molecular level. For instance, discovering of pathogenicity islands (Pais or PAIs), which are pathogenicity islands that are clustered in 50,000 to 200,000 base pairs at bacterial genome. Many of these Pais are carried on plasmids. They have a property of pathogenicity responsibility²⁹. Indeed, it is obvious that bacteria found its way to inherent antibiotic resistance ability with time, the matter that exposes our health to a real danger⁷⁸.

The discovery and public use of penicillin led to the ending of work on dysentery phages in 1944. Despite penicillin having broad spectrum activity against wide range of bacterial strains, typhoid (*Salmonella typhi*) was not treatable by penicillin. These encouraged scientists to work again on phages as a substitutive solution²⁹. Penicillin is the first drug of choice to treat acute and relapsing tonsillitis. Although it is a potent *in-vitro* antibiotic agent, it exerted inability to eradicate GABHS due to many factors; mainly bacterial interactions, in which beta-lactamase-producing organisms help to protect GABHS from penicillin and due to broad spectrum killing activity that work on eradication of normal flora which act as a natural defense barrier. Other factors that cause failure of antibiotic therapy include development of bacterial resistance or drug tolerance, mistaken prescription followed improper diagnosis, wrong treatment, patients status and re-infection from carrier³⁰.

Reported study revealed the relation between inappropriate prescribing of antibiotics for treatment of acute tonsillitis cases and developing of bacterial resistance at Primary Care Practice (PCP) level, the study disclosed that treatment failure was resulted from inaccurate etiology determining and false prescribing of antibiotics due to low adherence or no adherence to national health guidelines³¹.

Worldwide consensus that finding of safe alternative treatment that replace antibiotics to combat resistant bacterial infections is a top priority, some might ask regarding this priority whether it should started from mild or severe infection? Because that many believe the therapy must begin for invasive cases³². For that, extensive trials like developing of medical bacteriophages, phage lytic enzymes or antimicrobial peptides

(AMP) had been addressed but they failed to bring the ultimate promising solution. An essay listed by Waldetoft & Brown (2017) focused on study of changing the path of finding the proper antibiotic alternative should begin from research on mild cases depending on two situations, the first, according to their questions, they found that relatively mild infections were responsible for the majority of antibiotic prescriptions than for severe cases, a rationale that led to growing of antibiotic resistance. Second, by focusing upon such these mild infections, this will contribute in resolving of resistance problem, thus increase in success of alternative medicine^{33,34}.

Evermore, scientific paper by Stanton in 2013 focused on emergence of antibiotic resistance problem and necessity for discovery of antibiotic alternatives, the study showed the urgent importance to find solution and thus discovery of new and more effective antibacterial agents is primordial⁵⁹.

WHO launched the first antibiotic awareness week in 2015. It warned about losing of antibiotics importance due to bacterial resistance that developed from dependence on well-known classes of antibiotics and their uncontrolled use, and if there is no upcoming solution, our world will face a danger of common infections with no treatment⁷⁸. At the same time, repeated handling trials and mistaken or improper diagnosis and treatment of tonsillitis, brings many dangers to patient health and widen the gap, added to side effects caused by chemically synthetic antibiotic and anti-inflammatory drugs. Altogether worsen our health and subsequently affect life. Hence there is an urgent need to explore potent safe anti-tonsillitis treatment that can be prescribed safely without risks of inappropriate diagnosis to replace old faulted treatment. Therefore herbal medicine seems to be proper solutions that motivate academic researchers and clinicians in the field to substitute.

Bacterial Resistance Impact Dimensions

Not that treatment effectiveness solely is the consequence of treatment resistance problem, the issue actually extended to many aspects, for instance and not to enclose, fateful impact, economic impact, environmental impact and work efficiency impact.

At present, antibiotic resistant bacteria

constitutes a real health care crisis, in which most of bacteria became multi-drug resistant⁷⁸. In 2013, CDC reported that two million of United States (US) people acquire serious infections by resistant strains each year, from those, at least 23,000 die every year. Moreover, 250,000 of people with *Clostridium difficile* infections require hospital care as a result of uncontrolled use of antibiotics, and about 14,000 of those patients die every year in US³⁵. Klevens et al. (2007) listed that the majority of deaths from cases of hospital-acquired infections (HAI) were by antibiotic resistant organisms³⁸. For example, in 2006, nearly 50,000 American patients were killed by sepsis and pneumonia (common HAI). These cost their country more than \$ 8 billion³⁹.

Another study by Filice et al. (2010) found that studies on the cost of antibiotic-resistant infections collected from US health care system ranges from \$ 21 billion to \$ 34 billion each year, added to more than \$ 8 million for additional hospital days, in which the burden of antibiotic resistant infection on each patient cost from \$ 18,588 to \$ 29,069 United States Dollar (USD)⁴. Each year the US health care system spent over \$ 20 billion per patient³⁷. Additionally, the hospital stays for cases suffering antibiotic-resistant infections increased from 6.4 to 12.7 days. It means that those patients are unable to work during this time, thus losing their salaries. The total costs due to these households reaches over \$ 35 billion each year.

In addition, CDC also suggested that it is difficult to estimate the exact costs due to many factors, such as: duration of treatment courses whether it is short or long, extended hospital staying period, extra health care uses and additional specialists' visits and advice, and that most of antibiotic-resistant infections need costlier treatments. Some estimates taken from health care system in US in 2008 revealed that direct health costs on economy reached about \$ 20 billion with extra \$ 35 billion for lost productivity to society³⁵.

More Dilemmas upon Synthesized Chemical Antibiotics and Anti-inflammatory Drugs

Common popular use of NSAIDs has lead up to arising and manifestation of adverse drug reactions which become popular everywhere. Many adverse drug reactions and side effects reported on use of NSAIDs such as increased

risk of gastrointestinal ulcers and bleeds, heart attack and kidney disease, tolerance, gastric lesions, interference with blood coagulation and many others that range from moderate to severe side effects^{40,41,42}. Many reports suggested that more side effects appeared with their frequent use, viz., cardiovascular like myocardial infarction and heart stroke^{43,44}, erectile dysfunction⁴⁵, inflammatory bowel disease (e.g., Crohn's disease or ulcerative colitis), renal side effects such as interstitial nephritis, nephrotic syndrome, acute kidney injury, acute tubular necrosis and renal papillary necrosis⁴⁶, photosensitivity and allergy.

In fact, due to reported undesired side effects of NSAIDs even at least extent, it is recommendable to apply use of medicinal plants instead⁴⁷. Anywise, chemical side effects not restricted on use of NSAIDs, even antibiotics reported multiple side effects and disadvantages which mentioned on the following table 1, hence as one of the main reasons, this article necessitated to substitute conventional chemically manufactured treatment by natural medicinal plant⁴⁸.

Traditional Herbal Medicine and Its Advantages as a Promised Solution

Preeminent medical systems had been used widely in South East Asian Region categorized within folk medical exercises, these include Yoga, Ayurveda, naturopathy, Unani and Tibetan medicine, in which reports reveal that 70-80

percent of population in this region using phyto-medicine. In Malaysia, there are three traditional medicines used widely, these are Traditional Chinese Medicine, Traditional Malay Healers and Traditional Indian Healers. Multiple synonyms of traditional medicine used widely all over the world these include: alternative medicine, complementary medicine, herbal medicine, phyto-medicine, non-conventional medicine, indigenous medicine, folk or ethno medicine and natural medicine⁴⁹.

National Center for Complementary and Alternative Medicine (NCCAM) categorized alternative medicine into Whole Medical Systems (such as Ayurveda, herbs and traditional Chinese medicine), Mind-Body Medicine (such as prayer, mental healing and therapies that use creative outlets), Biological Based Practices (like Herbs, vitamins and foods), Manipulative and Body-Based Practices (for instance Chiropractic Medicine and Naturopathy) and Energy Medicine (such as bioelectromagnetic-based therapies and electromagnetic fields)⁷⁶.

One of the oldest medical systems in the Indian subcontinent is Ayurveda. It is experienced since 12th century BC. Ayurveda system constitutes a way of life that look around fulfilment of physical, mental, social and spiritual well-being at the time that phyto-therapy (herbal therapy) constitute a major segment in this system⁴⁹. Herbal remedies have been a principle segment of human health care due to therapeutic effectiveness upon their

Table 1. Main disadvantages of broad spectrum antibiotics

Conventional Antibiotics

Multiple side effects, including intestinal disorders, allergies, and secondary infections (e.g., yeast infections) have been reported, If patient is allergic to antibiotic, treatment is very difficult.

Antibiotics exhibit bactericidal or bacteriostatic effects not only on the cause of bacterial disease, but to all bacteria of our body including normal flora. Thus their non-selective action affects the patient's microbial balance, which may lead to various side effects.

The broad spectrum activity of antibiotics may select for resistant mutants of many pathogenic bacteria species, Resistance to antibiotics is not limited to targeted bacteria.

Some antibiotics are bacteriostatic, i.e., they inhibit the growth of bacteria, rather than killing them (e.g., Chloramphenicol), their use give a chance to bacteria to develop resistance.

They are metabolized and eliminated from the body and do not necessarily concentrate at the site of infection, i.e. they are not specific.

Production is complex and expensive, Developing a new antibiotic (against antibiotic resistant bacteria) is a time consuming process and may take several years to accomplish.

constituents and classical medicinal plants have been used for thousands of years ago^{79,50}. Different human civilizations have their own medicinal plant library, in which some wise people become experienced practitioners and attend to have deep wisdom to deal with domestic plants⁵¹.

Ancient medical literature of our humanity disclosed that people used to deal with medicinal plants due to their obvious potent effects in both humans and animals and the traditional herbal medicine continued to gain its importance due to its wide therapeutic applications. It earns this prominence from plants' natural chemical composition, i.e. secondary metabolites. Some relative knowledge about many medicinal plants and their mechanism of action enables clinicians to use them as natural remedies⁵². Many antibacterial activity evaluating studies of selected edible plant extracts confirmed their potential actions against MDR bacteria^{60,61}.

A study performed by Al-Naggar & Chen, (2011) focused on nutrition and cancer prevention relationship, the study revealed the importance of human being to depend on natural diet as a result of dietary manipulation is considered in all reports to be the cornerstone of prevention and management efforts of the many mentioned diseases and natural sources of diet and medicines are of great value to natural health equilibrium⁶².

Medicinal plants have powerful experienced efficacy with no encountered side effects, for that higher majority of people tend to depend on them, and about 80% of worldwide people are on use of these plants for their primary healthcare needs according to WHO⁵³. Furthermore, one of the main factors that increase using of phytotherapy is due to poverty and natural widespread of plants on the earth, this availability reflects the easy ability of patients to get them. Studies performed by Prasad, Rajgopal, Kant & Badarinath, (1999) and Khan et al., (2014) mentioned some pros of these medicinal plants such as their low cost and ease of use away from complicated health systems and hard transportation facilities that obstruct the way^{54,55}.

Nowadays, we believe and trust in natural and organic products, particularly medicines from natural sources, due to desired potent actions and unwanted chemical side effects⁵⁶. In general,

medicinal plants have a diverse of chemical components which make them enormous therapies without chemical side effects.

At the end of 19th century, many laboratories tried to begin experiments of investigation on medicinal plants⁵⁷. Synchronously, human trials to explore new plants are continuous⁵⁸. In fact, many man-made drugs are of plant origin. *S. lappa* considered as one of the important medicinal plant that played a prominent role in phytotherapy field and widely used by various medical systems mainly ayurveda, but still there is a dearth of ultimate knowledge about medicinal use of *S. lappa* plant, for which reason its suggestion of use as treatment choice is destined to seek for its lethal effects of roots extract against tonsillitis causing bacteria particularly type A beta haemolytic *streptococci* in *in-vitro* model.

On the contrary, phytotherapy faced many problems and challenges and some people thought that it was not proven to give the same effects of synthesized drugs. These thoughts came from two reasons; the first is that related research in many fields was not enough to satisfy the reviewer due to unavailability of specialized phytotherapy centers and laboratories. The second is that the proven works still were not famous and widely known. Add to that, there was a little interaction and collaboration between practitioners who worked on understanding of botany and those who worked on therapeutic uses of plants.

Why Saussurea Lappa?

Reviewed literature about *S. lappa* disclosed that the plant possessed potent antibacterial and anti-oxidant activities. Antimicrobial activity of *S. lappa* resulted from its composition, particularly the hydroxyl (OH⁻) group in its structure which prevents bacterial growth by denaturation process, thus increasing cellular membrane permeability⁸⁰, which in turn cause rupture of cell membrane and death of bacteria⁶³.

Traditionally, *S. lappa* used by old Korean physicians to treat peptic ulcer, asthma, cough, pharyngitis, it is used as anti-inflammatory, anti-septic and anti-tumor agent too⁶⁴. *S. lappa* considered as one of the most widely used ethno pharmacological plant in Shopian forest of Kashmir⁷. *S. lappa* family is widely spread in India. It is useful in treatment of asthma, cough

and peptic ulcer according to ayurveda clinicians. Additionally, from the Indian literature, there are many drugs described by ayurveda classics which used in treatment of *Tundikeri* (disease that has same signs and symptoms of tonsillitis)⁶⁶.

From the Indian literature on treatment trials regarding tonsillitis, they experienced many management methods, such as using of oral medications added to local application of treatments like Gandusha and Kavala, and last treatment of choice is surgery⁶⁶. But according to ayurveda, combination of oral herbal drugs with local application of treatments can be useful even in cases of recurrent tonsillitis before ending fate of surgery.

Basically, roots have chemical composition of essential oils (1%), alkaloids (0.05%) and saussarine. these substances have many beneficial medical uses without side effects. For example, essential oil content has expectorant, antispasmodic and diuretic effects. Other ingredients include resinoids (6%), inulin (18%), saussurea lactones (20-25%), fixed oils and minor content of tannin and sugars. Even more, constituents of roots vary from Indian plant and from other countries sources. One of the amazing characteristics of essential oils is their powerful action against bacteria. A valuable overview of chemo-profile of *S. lappa* plant disclosed the main pharmacological constituents were cynaropicrin, saussureamines A & B, costunolide and dehydrocostus lactone.

Phytochemical studies of *S. lappa* revealed the presence of terpenes: mono-terpenes like anethole, thymol and camphor^{67,68}, sesquiterpenes: especially sesquiterpene lactones from plant roots essential oils⁶⁹, flavonoids: such as luteolin, rutin and apigenin⁷⁰, phytosterols: as lappasterol, anthraquinone compounds and many others. A chemo-profile of *S. lappa* was mentioned by details in reviews by Singh, Chahal & Singla in 2017^{71,72}.

In spite of potent bioactivities of folk plant medicines in facing of many diseases, total comprehensive profile of plants active ingredients have not been clearly mentioned because of their complicated chemical composition. However, part of chemical form that is responsible to induce anti-inflammatory properties have been suggested and reported by many researchers,

these compounds include alkaloids, flavonoids (the major anti-inflammatory agent), ligands, peptides, polyphenols, polysaccharides and saponins^{73,74}.

Many several *in-vitro* and *in-vivo* test models were done by related experts to investigate pharmacological properties of the *S. lappa* plant. In general, they deduced many of its activities such as anti-ulcer, anti-tumor, immunomodulatory, anti-inflammatory, hepatoprotective, antifedant, antibronchitis, hypolipidaemic, hypoglycaemic, anti-parasitic, and central nervous system (CNS) depressant activities and effects⁷². All of these explained, discussed and reported by related researchers in the field. A scientific review on *S. lappa* done by Pandey et al., (2007) brings many details of these actions organized accordingly⁷².

They knocked through and reported the anti-inflammatory properties of ethanol & methanol extracts of roots of *S. lappa*. For instance, methanol extract exhibited an inhibition effect of Cytokine Induced Neutrophil Chemotactic factor (CINC) initiation and suppresses nitric oxide synthase enzyme⁷⁵. Additionally, this extract exerts strong inhibitory effect on production of Tumor Necrosis Factor-alpha (TNF- α) and pro inflammatory cytokines. Yu et al., (2007) reported the inhibitory effect of ethanol extract of *S. lappa* on *Streptococcus mutans* which exerted a significant inhibitory action and prevent the bacterial growth and acid production at concentration of 0.5-4.0 mg/ml. Even at this concentration, ethanol extract exhibits anti-adherent activity on bacteria and inhibits formation of water-insoluble glucan⁶⁵. Yu et al., (2007) listed some activities of *S. lappa* on oral diseases, in which it manifests considerable therapeutic effects on dental caries, halitosis and periodontal diseases that are related to infection by *S. mutans*⁶⁵.

Different plants are varying apparently in distribution of phytochemicals and active ingredients in their different parts of plant accordingly³⁶. Many preceding ayurveda physicians informed that *S. lappa* roots are the main part of plant^{25,18}. This plant used broadly by locals for different purposes especially for respiratory tract illness. *S. lappa* roots are easy to handle (does not leak like a fluid), safe (not harmful or hazardous matter), cheaper and can be stored easily for future use.

In nutshell, many phytotherapy practitioners performed experiments suggested the potent positive effects of ayurveda plants in general against tonsillitis. These plants possess number of brilliant properties (such as their anti-inflammatory, anti-viral, anti-pyretic, anti-oxidant and anti-pain activities) that enable them to act as a broad spectrum drugs. These effects help together to treat such diseases with desired efficacy and safety.

DISCUSSION

Tonsillitis is disquieting disease toward its patients, its recurrent attacks disturbing life and distressing patients. Many cases around the world suffering the pain of tonsillitis which ranges from mild to severe pain in many cases, thus majority of cases tend to consume sedatives such as NSAIDs regularly with prescribed chemical antibiotics, in which both accompanied by their hazardous side effects. At the same time, fail of tonsillitis treatment that resulted over developed bacterial resistance to available antibiotics, enhance the reason to find a promised efficient solution assumed by testing of natural potent treatments that experienced without side effects

Conventional antibiotics endangers our normal flora, subsequently our health as mentioned. These jeopardies imperil livings on the planet as well as environment. Awareness of WHO and related organizations belled out the upcoming real danger of resistance problem and losing of antibiotics as antibacterial treatments, gives meaning to factual extent of impact and bring responsibility to find alternative safe drug. Actually, we need to decrease depending on chemical antibiotics gradually synchronized with offering and increasing use of safe substitutive medicines.

Meanwhile tonsillitis can present as viral or bacterial infection, simply looking and inspection at tonsils for diagnosis does not reveal the cause. Thus, prescribing antibiotics to wrong-viral affected patient as happen by many doctors is a medical mistake, for that there is need to treat by right choice drug, that must be active and potent against both causatives and preferable to hold local anti-septic effects, added to its guaranteed safety and its ease of prescribe and use by everyone as over the counter (OTC) drug. This gives a rationale

that many phytotherapy plants including *S. lappa* hold multi effective activities (like to be anti-bacterial, ant-viral and anti-septic) at the same time.

Indeed, ancient use of *S. lappa* by rural communities for a long time indicates that there are beneficial roles with no historical aforesaid side effects associated with its use with taken in mind's eye long term its use. Thereafter, according to results from researches and previous studies on *S. lappa* potent chemical composition, enhanced by evidences from literature review over a long time which informed that this plant possess a wide potent anti-microbial, anti-inflammatory and anti-septic bounce. Altogether, leads to a rationale that *S. lappa* can be used as an effective anti-tonsillitis treatment.

Exceedingly presentation of the extent of antibiotic bacterial resistance problem and the importance of herbal medicines as a prospective choice of antibacterial treatment, through review of previous and current literature as well as practical investigatory lab work will disclose more facts about advantages and disadvantages of both treatments when compared to each other.

CONCLUSION AND RECOMMENDATION

In conclusion, the world is moving towards losing of antibiotics, those marvel drugs that lived for decades to fight bacteria that were responsible to cause many diseases. Tonsillitis is one of those infections that have wide presence throughout the world. Previously and currently, it was treated by broad spectrum antibiotics. Researchers in related fields, due to developed bacterial resistance and ineffective treatment seek for alternative safe treatments and many believe that solution lay in depending on herbal medicines; they depended on rationale of their safety and potency. This paper focus on future need of evaluating (by lab work) of *S. lappa* roots extract as an effective safe herbal remedy for acute tonsillitis cases whose infected mainly by bacteria.

To help in elimination of antibiotics crisis and to replace them by safe treatments we need to evaluate specific natural herbal treatment (*S. lappa*) whether it is effective and safe or not toward particular case (tonsillitis bacteria), there is an urgent need to initiate lab experiment studies for such testing. The prospective collected

information and results supposed to contribute in the richness of herbal pharmacy medicines and biomedicine libraries as well as adding knowledge for new researchers in the field and to open a new door for natural therapy for such cases to overcome developed antibiotic resistance problem.

Evaluation of anti-bacterial and anti-inflammatory activities of *S. lappa* roots extract against tonsillitis bacteria then determination of specific concentration for extraction which presents the peak activity, this will help in affording of potent treatment for tonsillitis cases, and importantly to decrease depending on antibiotics at least at tonsillitis level, and will share in diminishing bacterial resistance issue. Testing and evaluation of toxic effects of the plant extract will help in offering safe drug easy to prescribe (or self-prescribed) to all types of tonsillitis cases without risk of side effects of existing prescribed drugs and without risk of wrong diagnosis or prescribing.

Moreover, *S. lappa* owns antiseptic effects beside its proposed anti-microbial and anti-inflammatory effects. Hence, due to all previously mentioned justifications, this article attempts to focus on *S. lappa* as an important potent medicinal plant to help in relieving condition of acute tonsillitis. It is recommended to focus on testing of different ethanol extract concentrations from *S. lappa* roots against β -hemolytic *streptococci* type-A bacteria by *in-vitro* laboratory experiment to evaluate the effectiveness. Medically, using this herb for treatment of acute tonsillitis, this supposed to add extra prospective medical effects added to treatment course by collecting of anti-bacterial, anti-inflammatory and anti-septic effects in one agent. It will be incredible if the plant exerts an anti-viral and anti-fungal effects too in the future.

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CONFLICT OF INTEREST

The authors declares that there is no conflict of interest.

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