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Ethnomedicinal, Pharmacological and Commercial Perspectives of *Laccifer lacca* Body Exudate (LBE)

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Abstract: Nature-derived products have been serving humanity from ancient times in many aspects such as food (honey & wax products from bees), textiles (silk from silkworms), and various kinds of pollination in flowering plants. Undoubtedly, people cannot forget their benefits to our daily life, except above benefits insects have a great potential in the form of folklore medicines. LBE is a resinous secretion of a scale insect commonly known as Lac Insect (*L. lacca*) as a protective coating on the outer surface of many kinds of trees, including Ber (*Ziziphus marutiana*), Kusum (*Schleichera oleosa*), Palas (*Butea monosperma* syn. *frondosa*). The review highlights the coverage of natural product chemistry and ethnomedicinal and commercial perspectives on natural products obtained from LBE because of recent literature exploration.

Keywords: *Laccifer lacca*; natural medicine; natural product; resin; alternative medicine; Unani medicine; Ayurvedic medicine.

1. Introduction

Herbal products as medicines are chiefly utilized as alternative methods curing several kinds of acute and chronic disorders/diseases. These medicines have found their potential to decrease the side effects and, thus, can be believed to be safer than their synthetic counterparts (Allopathic preparations and formulations). Interestingly, several nature-derived formulations have shown vast significance in treating various diseases and ailments in ancient times and the present scenario [1]. Nowadays, we have used extensively natural products in our daily lives since prehistoric times. Nature derived products have been serving humanity from ancient times in many aspects such as food (honey & wax products from bees), textiles (silk from silkworms), and various kinds of pollination in flowering plants; except above benefits, insects have a great potential in the form of folklore medicines [2,3] and sometimes food supply chain due to specific edibility of some insects. Insects meet the human nutritional requirements, making them a brilliant nutrition diet of humans, containing minerals such as Na, K, P, Ca, Mn, Fe, Cu, Zn certain carbohydrates, high protein, mono- and polyunsaturated fatty acid contents [4]. Recently, the human-insect relation with potential bioengineered applications emerged to their utilization in various sectors like alternative medicine, derived and semi-

synthetic drugs. However, the public perception about insects amongst the human community is not found so consistent, and therefore, the need must be raised for improving the profiles of beneficial insect species. The most important provisioning ecological, economic, and commercial services of the beneficial insects concerning the *L. lacca*, are natural products, pollination, drugs, etc. [1-5]. This article overviews the ethnomedicinal and commercial perspectives of natural product-resin obtained from *L. lacca* as Body Exudates.

2. Descriptionand distribution

LBE is a resinous secretion of a scale insect commonly known as Lac Insect (*L. lacca*) as a protective coating on the outer surface of many kinds of trees, including Ber (*Ziziphus marutiana*), Kusum (*Schleichera oleosa*), Palas (*Butea monosperma* syn. *frondosa*). About 113 varieties of host plants are mentioned as a lac host plant. Lac insects thrive on twigs of certain plant species (host plants), suck their sap, and grow, all the while secreting resin from their bodies. The chief host trees for the propagated life cycle of *L. lacca* are given in Table 1 [6,7]. Table 2 depicts the vernacular naming system of *L. lacca* insect,one of the most common scale insects belonging to a bug family *Kerriidae* under the superfamily *Coccoidea*[7].

Table 1. Host plants and trees for *L. lacca* insect.

Host **Plants/trees**	**Associated country**
Schleichera oleosa (Kusum) *Acacia arabica* (Babool) *Acacia auriculiformis* (Akashmani) *Acacia catechu* (Khair) *Albizzia lebbek* (Siris/Gulwang) *Butea monosperma* (Dhak) *Cajanus cajan* (Arhar) *Flemingia macrophylla* (Bholia) *Ficus benghalensis* (Bargad) *Ficus religiosa* (Peepal) *Grewia teliaefolia* (Dhaman) *Shorea talura* (Sal) *Ziziphus mauritiana* (Ber) *Zizyphus xylopyrus* (Khatber)	India
Albizia saman (Rain tree) *Cajanus cajan* (Pigeon pea)	Thailand
Cajanus cajan (Pigeon pea) *Hibiscus* species	China
Jatropha curcas (Barbados nut)	Myanmar, Mexico

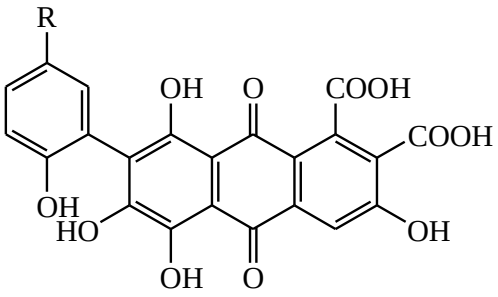
Table 2. Scientific classification of *L. lacca* insect with vernacular names.

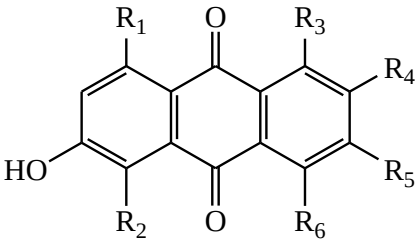
Scientific Classification		**Vernacular names**
Kingdom	Animalia	Hindi : Lakh
Phylum	Arthropoda	Sanskrit : Laksha
Class	Insecta	Tamil : Komburrki
Order	Hemiptera	Telugu : Kommolakka, lakka
Suborder	Sternorrhyncha	Malayalam : Ambalu, Arakku
Superfamily	*Coccoidea*	Bengali : Gala
Family	*Kerriidae*	Gujarati : Lak
Genus	*Laccifer* or *Kerria*	Sindhi : Joua
Species	*lacca*	English : Lac Arabic : Luk
		Persian : Laak
		Portuguese : Laca

At present, states of India produce LBE about 90% of Jharkhand, Bihar, West Bengal, Madhya Pradesh, Chattisgarh, Eastern Maharashtra, and northern Orissa Indian lac production. From ancient times, India exported LBE as a traditional red dye to many other countries (mainly between the 1700s-1800s). In the mid-1950s, India annually produced about 50,000 tons of sticklac and exported about 29,000 tons of lac; by the late 1980s, the figures were about 12,000 tons and 7,000 tons, respectively, due to the advent of synthetic dyes [6]. LBE is currently produced in the majority, including India, Myanmar, China, Thailand Mexico. The lac insect grows on the twigs of certain trees native to India and Southeast Asian Countries like Thailand and China. The species is assumed to be the most economical and commercially imperative due to the high-level exudates with various significant natural products, especially dye/pigment, resin with several therapeutically important substances [2,6].

3. Phytochemistry

The phytochemical investigations on LBE as powered lac showed the presence of several phytoconstituents such as carbohydrate, polyphenols, resins, alkaloids, and tannins chiefly [8,9]. LBE contains other minor chemical constituents. The biologically active molecules present in LBE are responsible for their usage in alternative systems of medicines. In the aromatic polyphenols class, many anthraquinone derivatives are present in LBE. Common anthraquinones, laccaic acids, and erythrolaccins found in LBE are presented in Fig. 2.





	R		R1	R2	R3	R4	R5	R6
Laccaic acid A	$-CH_2CH_2NHCOCH_3$	Laccaic acid D	-OH	-OH	-	-	-OH	-H
Laccaic acid B	$-CH_2CH_2OH$				CH_3	COOH		
Laccaic acid C	$-CH_2CH(NH_2)COOH$	Erythrolaccin	$-CH_3$	-OH	-OH	-OH	-H	-OH
Laccaic acid E	$-CH_2CH_2NH_2$	Desoxyerythrolaccin	$-CH_3$	-H	-OH	-H	-OH	-H
Laccaic acid F	$-CH_2CH_2OCOCH_3$	isoerythrolaccin	$-CH_3$	-H	-OH	-OH	-OH	-H

Figure 2. Common anthraquinones: laccaic acids and erythrolaccins found in LBE.

4. Ethno-medicinal and Pharmacological Activities

According to the Unani literature, *L. lacca* body exudates have numerous medicinal applications like a hemostatic, siccative, liver tonic, contraceptive, anti-inflammatory, anti-bilious, stomachic, aphrodisiac, anti-obesity, expectorant, kidney tonic, emmenagogues and also have beneficial use in obesity, hyperlipidemia, renal, hepatic, spleen disorders, jaundice, ascites, backache, premature ejaculation, leprosy, cough, hemiplegia, asthma, hemoptysis, epilepsy, chickenpox, ulcerations, worm infestation and palpitation [10].

4.1. Antifertility activity.

Agents that prevent fertility are called antifertility. Females' menstrual cycles and ovulation are affected and influenced by these medicines. The combined form of Estrogen and

progesterone are given as birth control pills. If an antifertility agent prevents fertilization, ovulation, implantation, and damages the zygote or causes abortion in females, it is considered a contraceptive [11]. Various plants are also available that have antifertility activity [12]. Other than plants, a recent finding suggested the insect body exudate also has antifertility activity. An animal study also revealed the antifertility activity of LBE. It was well known that there are various side effects of using contraceptives like side effects such as obesity, liver function derangement, liver adenomas, thromboembolism & disturbances in lipid and carbohydrates metabolism (bloating) and contraindicated in some conditions like jaundice [13], while LBE shown deviation from these side effects. Aisha et al. revealed the antifertility activity of LBE using an animal model. After completing the study, it was observed that LBE disturbed the estrus cycle in rats, thus interfering with the normal ovulation process as it prolongs the diestrus phase. Results also show that it prevents implantation and has a teratogenic effect due to its estrogenic effect [10]. Another study has shown its antifertility potential to a significant extent due to its estrogenic nature leading to the disruption of ovum production, maturation, and ovulation by changing the ovaries disposition of female rate [14].

4.2. Anti-obesity activity.

Obesity is one of the most increasing global public health issues. A major risk for developing comorbidity like type 2 diabetes, cardiovascular disease, joint and muscular disorders, gastrointestinal disorders, respiratory problems, and psychological issues in obese patients may affect their quality of life and increase mortality [15]. Researchers also found that obesity is directly associated with mortality that may decrease the life expectancy from 5 to 10 years [16].

Seedlac and shellac are very famous among Unani practitioners for their anti-obesity effects. Lac insects secrete the resinous substance on the branches of the host tree. These branches are cut and harvested as sticklac. Impurities are removed from the seedlac by crushing and sieving the crushed materials. The obtained product is known as “seedlac” although still, it contains 3-5% impurities. These impurities are removed by the heating and filtration process, and the final product is known as “shellac” [17]. An animal study was conducted using the formulations of these substances, and their anti-obesity effect was evaluated against high-fat diet-induced obesity in male Wistar rats [18]. In this study, these formulations significantly decreased the level of serum leptin, triglycerides, and increasing body weight was also prevented in the treatment group compared to the high-fat diet groups. The weight-reducing properties of LBE could be a promising alternative to control obesity.

4.3. Hepatoprotective activity.

The liver performs the largest functions among all the human body organs. The majority of the substances are metabolized by the liver, including drugs and food matters. The pharmacokinetics of the drug are also affected by the liver. The orally administered drugs have to follow first-pass metabolism and protein-bound and non-bound drugs metabolized by the liver. Thus, pharmacokinetics and pharmacodynamics depend upon the functions of the liver [19]. When the liver becomes damaged beyond repair termed liver failure. Drugs are the 4th most important cause of liver disease in Western countries [20]. Chronic liver disease or injury is a severe health issue that affects people worldwide. Fatty liver, hepatitis, fibrosis, liver cirrhosis, and hepatocellular carcinoma are the pathologic states of the liver diseases that

contribute to chronic liver diseases. Presently synthetic agents' efficacy in treating chronic liver disease is inadequate, and they have severe side effects. Various plant species and phytochemicals have been studied to treat chronic liver disease as an alternative [21]. An Unani formulation containing LBE named "Majoon-e-Dabeed-ul-ward" (MD) is available in the market. This formulation is popular due to its hepatoprotective effect. The efficacy of MD was evaluated using an acetaminophen-induced liver-damaged animal model. Increased levels of aspartate transaminase (AST), alanine transaminase (ALT), serum alkaline transaminase (SALP), lactate dehydrogenase (LDH), bilirubin, albumin, urea and creatinine confirmed the hepatic damage after acetaminophen administration. Increased level of lipid peroxidation is directly related to the reduced glutathione levels, adenosine triphosphatase (ATPase), and Glucose-6-phosphatase (G-6-Pase). Animals treated with MD shown significantly restored the level of above mentioned biochemical. Hence this study revealed the hepatoprotective activity of LBE containing herbal formulation against acetaminophen-induced liver damage [22].

Another animal study was conducted on albino rats, and the hepatotoxicity was induced using carbon tetrachloride (CCl_4). The hepatoprotective activity of a non-pharmacopoeial compound formulation containing LBE was evaluated. Biochemical parameters like SGOT (AST), SGPT (ALT), Alkaline phosphatase (ALP), total bilirubin, total protein, and antioxidant activity were examined before starting the treatment of the test drug. Silymarin was used as a standard hepatoprotective drug. From the above study, the biochemical parameters were estimated. Results showed that the formulation prevented CCL_4 induced elevation of serum ALT, AST, ALP, total bilirubin, and total protein level. Lipid peroxidation also decreased, and hepatocytes regeneration was also observed after using test formulation. This study revealed the significant anti-hepatitis activity LBE containing formulation compared to silymarin [23].

4.4. Anticancer activity.

In cancer cells, genetic lesions are irreversible and typically result in gene expression misregulation. The flexibility in the epigenome technique provides an opportunity to manipulate gene expression [24]. Epigenetic reprogramming could result in restoration with lower drug resistance of a more differentiated and less proliferative [25].

The chemical constituents of *L. lacca* are various Laccaic acids. It acts as a competitive inhibitor of DNA methyltransferase I (Dnmt I), thus representing potent anticancer activity and a better class of Dnmt inhibitors [26]. DNA methylation can be optimistic in cancer therapy; it can be achieved by reversing epigenetic programming. The treatment mechanism is based on gene expression; mostly 10 similar biological pathways are involved in cell adhesion and signaling [27]. LBE is novel and is a lead compound for polytherapy agents, a DNA-competitive inhibitor of Dnmt1 [28,29].

4.5. Anti-arthritic activity.

Osteoarthritis is the most prevalent joint condition globally, affecting more than 32.6 million people in U.S. adults, out of which 65% of people with this condition are women. More than 25% of adults around the globe who are older than 40 have Knee Osteoarthritis [30]. The symptoms of this ailment are similar to those of *Janusandhigatavata* in Ayurveda [31]. Modern medicine still does not have a comprehensive cure for this condition;thus, the treatments employed are mostly analgesics, anti-inflammatory drugs, and steroids, which do not cure the disease but only treat the symptoms [32]. Furious side effects such as gastritis, ulcers of the

mucosal layer of the stomach, heartburn, and vomiting, on the other hand, are listed as undesirable outcomes [33]. Sandhivata is provided as a Vatavyadhi in Ayurveda, and it is also considered that any sort of pain cannot exist without Vata. Sandhivata is initially mentioned by Charaka as "Sandhigata Anila" with symptoms of Shotha, which feels like a sack filled with air when palpated, and Shula on Prasarana and Akunchana (pain on flexion and extension of the joints) [34].

As a result, Sandhivata can be classified as a joint condition with Shula symptoms that worsen with movement, Shotha, and eventually full mobility restriction. Rajoria conducted a clinical trial based on demographic data like age, sex, type of work, socio-economic status, and diet. In reality, it appears that no single mechanism is completely to blame. The combination of Laksha Guggulu, Snehana, Swedana was responsible for the patients' total clinical recovery. Clinical symptom alleviation notably leads to functional recovery, and the patient becomes more functionally competent. All of the patients tolerated the medications and practiced well, and no adverse or toxic effects were seen in any of them [32-34].

Researchers had claimed that the formulation of *lakshagugglu*, *swedana*, and *snehana* showed significant improvement in a patient diagnosed with knee osteoarthritis, the overall impact of the treatments was mild, moderate, and maximal in groups A, B, and C, respectively, according to the clinical evaluation [34].

4.6. Bone healing property.

A Colles' Fracture is a major fracture of the forearm's radial bone near the wrist, leading to an upward (posterior) dislocation of the radial and a visible deformity. Even though the fracture occurs in the distal radius, not the wrist's carpal bones, it is usually referred to as a "broken wrist" [35]. The fracture is caused by a fall on the extended hand, and it is frequently accompanied by distal fragment dorsal and radial displacement and radial-ulnar articulation disruption. The ulnar styloid may be broken. The distal fragment and fractures communicate with the joint surface in some of these fractures. One of the most common and difficult outpatient fractures is the colles' fracture [36]. Completely healing of colles' fracture takes around 8-9 weeks, and to ensure the healing, it requires time to time X-Rays. The injured wrist and the fingers, hand, and shoulder on that side may be stiff for several weeks after the cast or splint is removed. As a result, exercise and physical treatment are required [37].

Though there are different devices or materials to immobilize the portion, its concept is the same as Sushruta mentioned for fracture therapy. So the herbal plaster, Lakshadi plaster, was used to achieve the goal of immobility. *Lakshadi* plaster is comprised of different ingredients like resin of *L. lacca*, *Cissus quadrangularis* Linn., Fuller's earth, Talk Powder, CommiphoramukulEngl, *Aloe vera* Linn [38].

5. Commercial Perspectives

5.1. Dyes and pigments.

Lac is being used for a long time and is probably the most ancient insect dye. From prehistoric times, lac, henna, madder, and many more dyes of natural origin have been extensively used to dye textiles, clothing, wood, body parts, wall paintings, etc. [3,39-42]. Sample detection and analytical techniques have revealed that during the Ottoman Empire's progression in the 15th century, lac dye had been widely known to obtain crimson to scarlet red coloring [43]. The dyeing with natural colors, particularly with lac, madder, cochineal, and

henna was used by Europeans also documented. The coloring component is recognized as stick lac in the commercial market, the resinous protective secretion of tiny lac insect *L. lacca.* Chemically, the presence of several anthraquinones (Fig. 2) with an average molecular weight of ~500 Da and active chromophoric functional groups such as –OH, -COOH, -$NHCOCH_3$ etc., make LBE a brilliant dye. The anthraquinones, collectively called lac dye, are readily soluble in acidic (~pH=2-3) lukewarm water and can dye wool and silk directly, giving a beautiful orange-red shade that is fast to washing and light. [44]. Laccaic acids A and B are the principle dye components of LBE, whereas laccaic acid C, D, E, and F have been isolated in small quantities imparting varieties of red color on textile substrates [45-47]. Laccaic acid represents about 0.5-0.75% by weight of crude stick lac [48]. The insects secrete a thick resinous fluid that envelope their bodies; the secretions from insects coalesce and form hard continuous encrustation over the surface of the twigs, which can be refined into the shellac and other products. For commercial purposes, lac dye is obtained by extracting stick-lac with water and sodium carbonate solution and precipitating with alum or lime.

5.2. Resin and gum.

Thousands of forest dwellers, particularly in the central and western Indian states, depend on resins and gums as a viable source of income. Resins and gum from *L. lacca* are known as natural resin and gum that comes under the terminology Non-Wood Forest Products (NWFP), and they have been known to human civilization since time immemorial. The resins and gum have been utilized as superb trade materials in ancient times. The reason behind the highly accepted global importance of LBE is that it has a vital role in livelihood security of forest dependants, tribal economy, commerce, and traditional system of medicines, even they are used till now in Ayurveda, Unani, and Homeopathy [49-54]. These days gums find their use in paper, textile, confectionaries, and cosmetic industries due to their ability to stabilize emulsions, retain moisture and impart a smooth texture. In India, trees that exude gum and resins are plenty, and LBE is one of them.

5.3. Wax.

From the beginning of the 17th century, vast amounts of lac-based wax were exported to European countries, where it was chiefly used as sealing wax. LBE is also associated with the production of lac-based natural wax. Chemically, the wax obtained from LBE is a solid ester of fatty acid derived from shellac resins that contain ~3-6% as a byproduct during the shellac processing [51-53].

5.4. Honeydew.

In general, honeydew, particularly common as a secretion in hemipteran insects and is often the basis for trophobiosis and is a sticky liquid enriched with carbohydrates/sugar. The common secretor scale insects of honeydew are cicadas and lac insects [54-56].

6. Conclusion and Future Outlook

LBE is a resinous secretion of a scale insect commonly known as Lac Insect (*L. lacca*) as a protective coating on the outer surface of many kinds of trees, including Ber, Kusum, Palas, and many more. LBE contains phytoconstituents, main anthraquinones with an average molecular weight of ~400-500 Da, and active chromophoric functional groups such as –OH, -

COOH, which are associated with the dyeing, ethnomedicinal, pharmacological, and therapeutic potential, including *L. lacca* body exudates have numerous medicinal applications like a hemostatic, liver tonic (hepato-protective), contraceptive, anti-inflammatory, anti-bilious, stomachic, aphrodisiac, anti-obesity, expectorant, kidney tonic, emmenagogues and also have beneficial use in obesity, hyperlipidemia, renal, spleen disorders, jaundice, ascites, backache, premature ejaculation, leprosy, cough, hemiplegia, asthma, hemoptysis, epilepsy, chickenpox, ulcerations, worm infestation, and palpitation properties. Being of natural origin with minimal toxicity and high benefits giving access to workable quantities of pharmacological and therapeutics, LBE may deliver advances in alternative medicines coupled with genomics and bioinformatics that can pave the new way to possible future strategies of productions of the compounds originating from this diversity. To make a greener globe, the present scenario demands biodiversity-based drug targets, but there is still a need for systematic strategies for further applicabilities.

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Conflicts of Interest

The authors declare no conflict of interest and approve the final submission of the manuscript.

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