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Pharmacognostic, analgesic and antimicrobial screening studies of *Eugenia jambolana* seeds - An overview

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Abstract

The Medicinal plant products are becoming popular worldwide because they are known for their efficacy and safety (Heidari *et al.,* 2007). Thus, there is a dire need for the accurate and up-to-date information of medicinal agents. *E. jambolana* Linn. has been traditionally used for the treatment of various ailments. Thus, this plant was selected for the review of the antimicrobial and analgesic activities. It is concluded that the seeds of *E. jambolana* showed good analgesic and antimicrobial activities due to the presence of anthocyanin compounds.

Keywords: *Eugenia jambolana* seeds, Pharmacognostic, Analgesic, Antimicrobial study, Medicinal plants

Introduction

Natural flora has been a source of protective force for thousands of years. Natural products play an important role today for many pharmaceuticals (Balick *et al.,* 1996). Medicinal agents have been tried remarkably in concern of renewed global interest to find the novel lead molecules which are free from side effects. It is a common belief that natural medicines are safer than the synthetic pharmaceutical drugs which are toxic and possess several adverse effects. According to WHO report, 70-80% of the world's population relies on non-conventional medicine mainly from herbal sources in their primary health care (Rakh and Chaudhari, 2010). Moreover, the use of herbal drugs is increasing day-by-day. The most difficult aspect of medicinal practice is the management and treatment of pain which is the major symptom of various diseases such as osteoarthritis, central nervous system (CNS) disorders, gastrointestinal (GIT) disorders, etc. The analgesics and anti-inflammatory drugs such as NSAIDs are commonly used for the relief of pain and inflammation such as rheumatoid arthritis, osteoarthritis, etc and so are termed as pain relieving drugs. Analgesic therapy is now-a-days dominated by two major classes of drugs, namely, steroidal and non-steroidal anti-inflammatory drugs (NSAIDs). Both the classes produce serious side effects, such as, gastrointestinal disturbances or gastrointestinal irritation, kidney damage, respiratory depression, constipation and possibly physical dependence (Domaj and

Glassco *et al.,* 1999; Dahl *et al.,* 2000). Even today, many of the analgesics available in the market present various undesired effects that limits their clinical usefulness (Heidari *et al.,* 2007; Girard *et al.,* 2008). Therefore, the novel and better compounds are in much demand (Heidari *et al.,* 2006; Tao *et al*., 2008). The chemotherapy of the infectious diseases has been proved to be a continuous struggle for many years and the control of various diseases was confined to symptomatic cure which included personal hygiene, isolation of patient and good health. Microbial chemotherapy started with the vaccination discovered by Edward Jenner, but originally the term 'chemotherapy' was coined by Paul Ehrlich who discovered the first effective chemotherapeutic agent popularly known by the name Arsphenamine/Salvarsan, which opened the door to the future development in chemotherapy and antibiotics. Antibiotics represent the medicinally important group of secondary metabolites, which have been useful in our battle against infectious diseases. It was the discovery of wonder drug, Penicillin that revolutionized the field of antibiotics and directed the interest of the researchers towards the natural resources having different biological activities. Now-a-days, the bacterial resistance is spreading throughout the world steadily decreasing the potencies of prevalent antibiotics. Antimicrobial drug resistance may occur due to a pre-existing factor in the microorganisms or it may be due to some acquired factors by genetic changes or non-genetic mechanisms (Shah, 2005). Multiple drug-resistant microorganisms have increased around the world (Gould, 2009) and pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Staphylococcus aureus* (VRSA) are becoming resistant to almost all clinically available antibiotics (Zhang *et al.,* 2006; Livermore, 2009). The emergence and spread of antimicrobial resistance is an array of problems caused by various interconnected factors, many of which are related to overuse and misuse of antibiotics (Overbye and Barrett, 2005). This demands the development of new antimicrobial compounds to answer the problem posed by resistant and other microorganisms. Natural resources, especially actinomycetes, fungi and plants have been a rich repository for producing various antimicrobial agents. Recent years have witnessed a renewed interest towards exploring plants for developing the potent antimicrobial agents with better efficacy and minimal side effects to fight microbial diseases (Girish and Satish, 2008). The worldwide use of plants and their bioactive compounds has been well documented in literature for their different health benefits e.g. anti-cancer, anti-hypertension, anti-hypoglycaemic, anti-oxidant and antimicrobial activities (Bandyopadhyay *et al.,* 2004). Therefore, it is necessary to establish the scientific basis for the therapeutic uses of traditional plant products. The great Northern region of India and its herbal richness cater to the needs of modern medicine. This diversity of the Northern region, if used effectively and scientifically, it can provide a new drug molecule which may combat the adverse effects of the synthetic drugs used worldwide as well as reduce the cost of the medication. So, these facts if used further can be useful in treating many dangerous diseases. Especially, herbal plants have proven themselves a strong contender in acting as natural resource for bioactive compounds, such as *Taxus brevifolia* (Houghton *et al*., 2007), *Gingko biloba* (Goktas *et al*., 2007). Therfore, the herbal plants got importance and became essential ingredients of the various medicines of traditional Indian system of medicine such Ayurveda, Unani and Homeopathy. Besides the availability of reports on analgesic and antimicrobial activities of some indigenous

medicinal plants, the medicinal flora of our country still remains virtually unexplored. Thus, in an attempt to develop potent medicinal agent to fight against infectious diseases and related pain, in the present study, evaluation of antibacterial and analgesic activity of seeds of Jamun (*Eugenia Jambolana* Lam.) is carried out. It belongs to the family Myrtaceae and is native to the Indian subcontinent. Jamun tree is famous for its different names and for its fruit called berries. Annually, this tree produces oblong and ellipsoid fruits called berries. They are green, when raw and purplish black, when fully ripe and are sweetish sour to taste and contains high percentage of nutrients such are minerals, vitamins, tannins and protein content in adequate amount (Paul and Shaha, 2004). The pharmacologically active phytoconstituents present are flavanoids, terpenoids, anthocyanins and tannins (Li, Zhang and Seeeram, 2009). Jamun is a plant with known ethnomedicinal uses. Before the discovery of Insulin, jamun was highly useful in the treatment of diabetes and is an integral part in various system of medicine (Helmstadter, 2007). The plant has gained importance as an herbal drug to cure several diseases such as viral infections, inflammatory disorders, allergic disorders, gastric ulceration, heart diseases, cancer, liver infections, diarrhoea and diabetes. But the analgesic and anthelmentic activities of *Eugenia jambolana* are not yet explored.

Eugenia jambolana

Eugenia jambolana Lam. is a large evergreen tree indigenous to the Indian subcontinent belonging to the family Myrtaceae (Figure 1 a,b). The tree is famous for its fruits and the colloquial names (Chemexcil., 1992) which includes *Syzygium cumini*, *Syzygium jambolana*, *Eugenia cuminii*, Java plum, Portuguese plum, Malabar plum, black plum, Indian blackberry, jaman, jambu, jambul and jambool are attributed to the fruits (Warrier *et al.*, 1996).

Figure 1(a): *Eugenia jambolana* tree.

Figure 1 (b): *Eugenia jambolana* berries

Distribution of *E. Jambolana*

E. jambolana is native to the subtropical Himalayas, India, Sri Lanka, Malaysia and Australia, where it is widely cultivated. The tree was introduced from India and tropical Asia to southern Africa for its edible and attractive purple-red fruits. Now grown throughout the tropics and subtropics, the best forms are frequently cultivated in Java and Florida (Warrier *et al*., 1996). *E. jambolana* is one of the most widely distributed trees of India, occurring in the major forest groups except in the very arid regions. It is present in both moist and dry situations, occurring in the tropical wet evergreen forests, tropical semi-evergreen forests, tropical moist deciduous forests, littoral and swamp, tropical dry deciduous,

tropical dry evergreen, subtropical broadleaved hills, and subtropical pine forests (Noomhio and Dahut,1996).The tree favours moist, damp or marshy situations, where it tends to form gregarious crops. It tolerates prolonged flooding, and once established, it can tolerate drought. In dry sites, it generally confines itself to the vicinity of watercourses. It can grow on shallow, rocky soils provided the rainfall is sufficient. It is frost hardy when mature and sensitive when young. Seedlings are readily killed by fire, but saplings and trees survive ground fires. In the Himalayan valleys, it ascends to about 1200 m and in the Nigrils to 1800 metres. The *E. jambolana* trees are native to the various countries like India, Malaysia, Myanmar, Philippines, Sri Lanka, Thailand, Algeria, Antigua and Barbuda, Australia, Bahamas, Barbados, Colombia, Cuba, Dominica, Dominican Republic, Ghana, Grenada, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Indonesia, Jamaica, Kenya, Martinique, Mexico, Montserrat, Nepal, Netherlands Antilles, Nicaragua, Panama, South Africa, St Kitts and Nevis, St Lucia, St Vincent and the Grenadines, Sudan, Tanzania, Trinidad and Tobago, Uganda, United States of America, Virgin Islands (US), Zambia and Zimbabwe (Noomhio and Dahut,1996).

Botanical description

Jamun is botanically known as *Eugenia jambolana* belonging to the family Myrtaceae and is a large evergreen tree found in tropical and subtropical regions of India. Jamun is 50 fts (8-15 mts) in height and possess a large crown. The bark is pale brown in colour, when young while the mature bark is scaly grey or darkish brown. The stem is forks or is multiple stemed. The leaves are elliptic to broadly oblong and opposite in fashion. The leaves are smooth, glossy, fibrous in nature and are 5-10 cm (2-5 inches) in length (Figure 1). The leaves have turpentine smell and are pointed at the tip and have prominent mid rib with many lateral veins which are parallel to each other (Warrier *et al*., 1996). The flowers are sessile, 7-12 cm long, white to pinkish in colour and are arranged in clusters of three at the stem tip, with memberanous petals. The berries are the fruits of jamun which are purplish black in colour, round or ellipsoid, 1-2 inches long with centerally placed single large seed (Figure 1 b). The process of fruit development takes about two months during which lots of changes occur in the composition and phytoconstituents. The raw fruit is green in colour and when mature turns black. The completely ripe fruit has a combination of sweet, mildly sour and astringent flavor and imparts purple color to the tongue (Warrier *et al*., 1996). The botanical studies have shown that in the Indian subcontinent there are two main morphotypes of Jamun and this is based on the morphological and organoleptic features.

- Kaatha jamun which are small and acidic to taste;
- Ras Jaman, those are oblong, dark-purple or bluish, with pink, sweet fleshy pulp and small seeds (Jabbar, Khan, & Jazuddin, 1994; Morton, 1987).

Species and varieties of Jamun

The species and varieties of Jamun are discussed below.

Species

The genus Eugenia comprises of 1,000 species of evergreen trees and shrubs, most of them being tropical in origin. Some of the old world *Eugenia* species is now placed in the genus *Syzygium*. It belongs to the family *Myrtaceae*. Many of these species yield edible fruits and some of these are of ornamental and medicinal value. A wild species *Syzygium frniticosum* with small edible fruits is grown as windbreaks. The large evergreen tree has small dark purple fruits with prominent elongated seeds. The fruit is an astringent (causing contraction of

body tissue) even when ripe. A popular fruit is the rose apple or gulab-jamun (*S. jambos*). It is found in South India and West Bengal. The tree is very ornamental. The fruit is yellow in colour, generally insipid in taste and has high pectin content (Noomhio and Dahut, 1996). *S. zeylanica*, small tree with edible fruits, is found on the Western Ghats and S. *malaccensis* (Malay rose apple) found in South India. Another related fruit found in South India is Surinam cherry (*S. uniflora*). It is a small tree with blight red aromatic fruits. *S. javanicum* (water apple) is also found in South India and West Bengal. *S.densiflora* is used as rootstock in jamun (*S. cumini*) and is resistant to the attack of termites (Noomhio and Dahut, 1996).

Varieties

There are no standard varieties of this fruit. The common variety grown under North Indian conditions is "Ram Jamun". It produces big sized, oblong fruits, deep purple or bluish-black in colour at full ripe stage. The pulp of the ripe fruit is purple pink and the fruit is juicy and sweet. The stone is small in size. The variety ripens in the month of June- July and it is very common both in rural as well as in urban markets. Another late maturing variety bears small sized, slightly round fruits, deep purple or blackish in colour at full ripe stage. The colour of the pulp is purple, less juicy, the weight and sweetness of pulp is also less in comparison to that of 'Ram Jamun'. The stone present in this variety is comparatively large in size. Fruits ripen in the month of August (Shafi, Rosamma, Jamil, & Reddy, 2002). At present, there are a number of seedling strains of jamun in India which provide a good scope for selection of better varieties (Noomhio and Dahut, 1996).

Table1: Taxanomical Classification.

Kingdom	**Plantae**
Division	Angiospermae
Class	Eudicots
Order	Myrtales
Family	Myrtaceae
Genus	Eugenia
Species	Jambolana

Phytochemistry

The pulp of Jamun is highly nutritive and it contains a variety of constituents such as vitamins include beta-carotene, thiamine, riboflavin and ascorbic acid. Jamun also contains minerals in varied compositions as Mg, Ca, Fe and Na (Paul and Shaha, 2004). Besides vitamins and minerals, it also contains carbohydrates such as glucose, sucrose, fructose, maltose, fibre content, protein content and moisture (Noomhio and Dahut, 1996). Eugenia is known to possess diverse phytochemicals having several health benefits. The medicinal constituents are present in different plant parts. For instance, the leaves are reported to contain beta-sitosterol, alpha-terpenol, myrtenol, cineole, geranyl acetone, alpha cadinol, pinocarvone and muurolol (Shafi, Rosamma, Jamil, & Reddy, 2002). Similarly, the stem bark is reported to contain friedelin, friedelan-3-alpha–ol, betulinic acid, kaempferol, beta-sitosterol-d-glucoside, gallic acid, ellagic acid, gallotanin and ellagitannin (Rastogi & Mehrotra, 1990; Sagrawat *et al.*, 2006). The flowers of *E. jambolana* contain oleanolic, ellagic acid, isoquercetin, myricetin, quercetin and kaempherol (Sagrawat *et al.*, 2006). The jamun pulp is reported to contain anthocianins, delphinidin, malvidin-diglycosides (Li, Zhang and Seeram, 2009; Sagrawat *et al*., 2006; Veigas *et al.*, 2007; Sharma, Viswanath, Salunke, & Roy, 2008; Sharma, Balomajumder, & Roy, 2008) and the seeds are reported to contain jambosine, gallic acid, ellagic acid, corilaginum, 3,6-hexa-hydroxyl-diphernoyl glucose, 3-galloyl

glucose (Rastogi & Mehrotra, 1990; Sagrawat *et al.*, 2006).

Analgesic study

Pain

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage". Although acute pain and associated responses can be unpleasant and often debilitating, they serve important adaptive purposes. They identify and localize noxious stimuli, initiate withdrawal responses that limit tissue injury, inhibit mobility, thereby enhancing wound healing, and initiate motivational and affective responses that modify future behaviour (Figure 2). The intense and prolonged pain transmission, as well as analgesic under-medication, can increase postsurgical/traumatic morbidity, delay recovery, and lead to development of chronic pain (Vadivelu *et al.*, 2009).

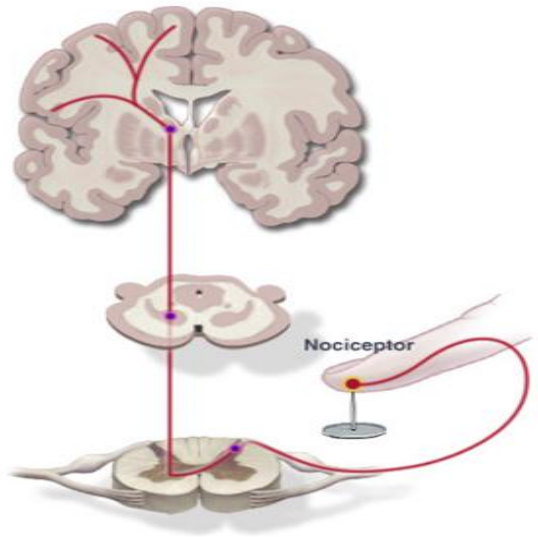

Figure 2: Diagram illustrating pain process.

Pain is a protective mechanism

Pain occurs whenever any tissues are being damaged, and it causes the individual to react to remove the pain stimulus. Even sitting for a long time on ischia can cause tissue destruction because of lack of blood flow to the skin where it is compressed by the weight of the body (Vadivelu *et al.*, 2009). When the skin becomes painful as a result of the ischemia, the person normally shifts weight subconsciously. But a person who has lost the pain sense, as after spinal cord injury, fails to feel the pain and, therefore, fails to shift. This soon results in total breakdown and desquamation of the skin at the areas of pressure (Almeida *et al.*, 2004).

Classification of pain

Pain can be categorized according to several variables, including its duration (acute, convalescent, chronic), its patho-physiologic mechanisms (physiologic, nociceptive, neuropathic), and its clinical context (eg. postsurgical, malignancy related, neuropathic, degenerative).

- ***Acute pain***, follows traumatic tissue injuries, is generally limited in duration, and is associated with temporal reductions in intensity (Berry *et al.*, 2001).
- ***Chronic pain*** may be defined as discomfort persisting for 3–6 months beyond the expected period of healing (Berry *et al.*, 2001).
- ***Physiologic* pain** defines rapidly perceived non-traumatic discomfort of a very short duration. Physiologic pain alerts the individual to the presence of a potentially injurious environmental stimulus, such as a hot object, and initiates withdrawal reflexes that prevent or minimize tissue injury (Patel *et al.*, 2010).
- ***Nociceptive* pain** is defined as noxious perception resulting from cellular damage following surgical, traumatic, or disease-related injuries (Flor, 2002).
- ***Neuropathic* pain** is defined by the International Association for the Study of Pain as "pain initiated or caused by a

pathologic lesion or dysfunction" in peripheral nerves and CNS. Some authorities have suggested that any chronic pain state associated with structural remodelling or "plasticity" changes should be characterized as neuropathic. Neuropathic pain is usually constant and described as burning, electrical, lancinating, and shooting (Vadivelu *et al.,* 2009; Manchikanti and Singh, 2004).

Peripheral receptors

The propagation of pain is stimulated with the activation of physiological receptors, called nociceptors, primarily found in the skin, mucosa, membranes, deep fascias, connective tissues of visceral organs, ligaments and articular capsules, periosteum, muscles, tendons, and arterial vessels. The receptors correspond to free nerve endings and represent the more distal part of a first-order afferent neuron consisting of small-diameter fibers, with little or unmyelinated, of the A-Delta or C type, respectively. Their receptor fields can consist of areas ranging from small regions to regions measuring several millimeters in diameter, or even of more than one site in distant territories (Lemont *et al.*, 2000).

Neurotransmitters

Neurotransmitters are the chemical substances that allow nerve impulses to move from one neuron to another and are often found in synapses.

The neurotransmitters include:

- Substance P - thought to be responsible for the transmission of pain-producing impulses.
- Acetylcholine – responsible for transmitting motor nerve impulses.
- Enkephalins – Reduces pain perception by bonding to pain receptor sites (Almeida *et al.*, 2004).

Pain mediators

The different types of pain at different parts of the body arise as a result of infection or damage to tissue or tissues. Both the events initiate an inflammatory response that is intimately linked with pain. The passage of nociceptive impulses generated in the peripheral nerve fibers due to the noxious stimulus as heat, cold, touch or a pinch depends on the release of various neurotransmitters like Substance P, Ach, etc. These neurotransmitters either act peripherally or centrally. The examples of pain mediators include plasma kinins like bradykinin, serotonin, histamine, prostaglandins, leukotrienes, cytokines and neuropeptides (Sutherland *et al.*, 2000).

Nerve fibers

Primary afferent fibers are classified in terms of structure, diameter, and conduction velocity. These fibres are of 3 types:

1.) C type fibers are unmyelinated, ranging in diameter from 0.4 to 1.2 μm and have a velocity of 0.5–2.0 m/s.
2.) A-delta fibers are thinly myelinated, ranging in diameter from 2.0 to 6.0 μm and have a velocity of 12–30 m/s.
3.) A-Beta fibers are myelinated, with a diameter of more than 10 μm and a velocity of 30–100 m/s (Meyer *et al.*, 2008).

Pain control theories

Several theories have been proposed till now as follows:

1.) Specificity theory:

According to the theory, a specific stimulus has a specific receptor which stimulates a particular location in the brain. The specific location identifies the pain's quality. Thus, any noxious stimulus applied to the surface of the skin results in a pain sensation. The evaluation of the type of pain occurs in the brain (Dickenson, 2002).

2.) Pattern Theory:
A pattern or coding of sensory information is created by different sensations. This theory is faulty due to the number of different types of receptors proven to exist (Dickenson, 2002).

3.) Sensory Interaction Theory:
It is based on that the intensity of the stimulus and central summation were the critical determinants of pain. This theory proposes that pain is not a separate entity but results from the over-stimulation of other primary sensations (touch, light, sound, etc.) (Dickenson, 2002).

4.) Gate Control Theory:
It was proposed by Melzack & Wall in 1965 in which substantia gelatinosa (SG) in the dorsal horn of spinal cord acts as a 'gate' that only allows one type of impulses to connect with the second order neurons (Melzack and Wall, 1965).

Pain perception
A number of theories have been formulated to explain noxious perception. One of the earliest ideas, termed the *specificity theory*, was proposed by Descartes. The theory suggested that specific pain fibres carry specific coding that discriminates between different forms of noxious and non-noxious sensation. The *intensity theory*, proposed by Sydenham, suggested that the intensity of the peripheral stimulus determines which sensation is perceived. More recently, Melzack and Wall proposed the *gate control theory* and suggested that sensory fibers of differing specificity stimulate second-order spinal neurons (dorsal horn transmission cell or wide dynamic range [WDR] neuron), depending on their degree of facilitation or inhibition, fire at varying intensity. Pain sensation is a series of complex interactions between central nervous system and peripheral nervous system. It is governed by excitatory and inhibitory neurotransmitters released in response to the stimuli. Stimuli can be physical, physiological or both.

Sensation of pain is composed of four basic processes (Guyton and Hall, 2006):
A.) Transduction;
B.) Transmission;
C.) Modulation;
D.) Perception

A.) Transduction:
In transduction, the noxius stimuli are translated into the electrical signal. This happens at the peripheral receptor sites. It begins when free nerve endings located throughout the skin, muscle and viscera were exposed to exact quantity of mechanical, chemical or thermal noxious stimuli or injury. The result of injury is the local release of neuron chemicals which mediates the inflammatory process. Such chemical mediator includes leukotrienes, serotonin, nitric oxide, bradykinin, prostaglandins, histamine, substance P, thromboxanes, and platelet activating factor, protons and free radicals. These chemicals released either activate the nociceptors and are directly involved in producing pain, or causes a sensitization of the nociceptor response to natural stimuli. As a result, leads to a situation known as primary hyperalgesia (Figure 2). Bradykinin is released upon tissue injury and present in inflammatory exudates. Serotonin can also potentiate the pain induced by bradykinin and enhances the response of nociceptors to bradykinin. Serotonin has additional action in modulating the peripheral release of primary afferent neuropeptides that cause neurogenic inflammation. Mast cells upon degranulation releases platelet activating factor (PAF), which in turn leads to serotonin release from the platelets.

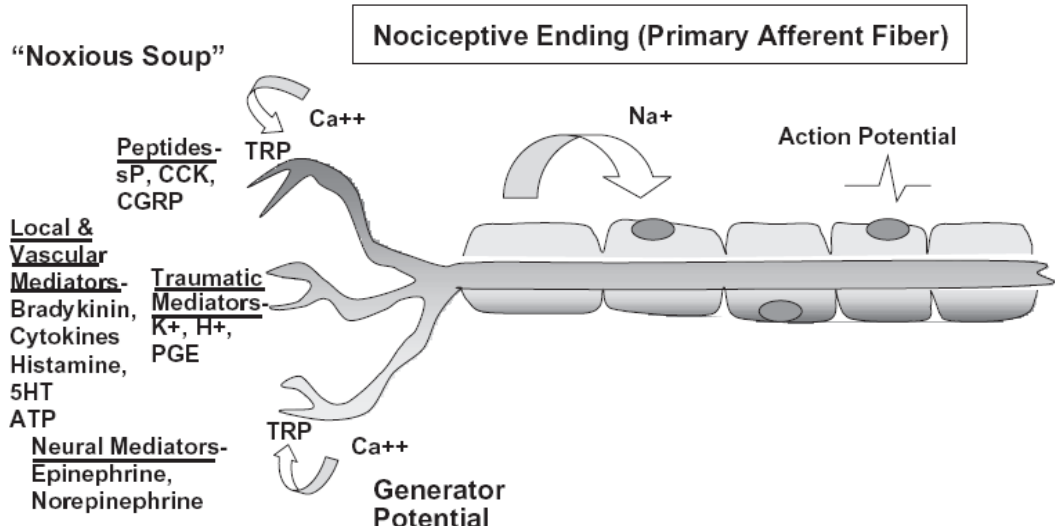

Figure 3: Noxious Soup Formation Following Tissue Injury.

Proton is selectively activated nociceptors and produces a sensitization of nociceptors to mechanical stimuli. Histamine is released from the mast cells when substance P releases from nociceptor terminals and it results in a variety of responses as vasodilatation and edema. Arachidonic acid metabolites as prostaglandins, leukotrienes and thromboxanes are collectively known as eicosanoids and their sensitizing effect plays a role in hyperalgesia. Subtance P, calcitonin gene related peptide and neurokinin are also included in these neuropeptides (Guyton and Hall, 2006). Following the tissue injury, cellular mediators activates the terminal nerve endings (nociceptors) of sensory afferent fibres, which leads to the release of peptides in and around the site of injury. Substance P causes further release of vascular mediators, thus increasing vascular permeability and nociceptor irritability creates a "noxious soup" that recruits adjacent nociceptors and results in hyperalgesia. Reflex sympathetic efferent responses releases noradrenaline which further sensitizes nociceptors.

B.) Transmission:

The next step is transmission which involves the propagation of electrical signals along the neural membranes. Prostaglandins and inflammatory mediators might change the permeability of the membrane; thus, produce an influx of sodium and efflux of potassium ions. As a result, depolarization of the neuronal membranes occurs. During depolarization, the electrical impulses are transmitted to the spinal cord via two primary afferent fibre types: myelinated Aδ-fibers and unmyelinated C-fibers. Aδ- fibers are responsible to conduct electical impulses that are associated with thermal and mechanical stimuli to the dorsal horn of the spinal cord rapidly (Table 1). While, unmyelinated C-fibers respond to mechanical, thermal and chemical stimuli and conduct electrical impulses to the spinal cord at a much slower rate compared to myelinated Aδ- fibers. When dorsal horn receptors are activated, electrical signals will be further propagated to the thalamus primarily via spinothalamic tract. From thalamus, signals are sent to cortex and brain for processing and interpretation (Berry *et al.,* 2001).

C.) Modulation:

The third step is the modulation of the information of nociceptive neurons from thalamus where the brain stem releases inhibitory neurotransmitters. For examples, nor-epinephrine, serotonin, Gamma-

aminobutyric acid (GABA), glycine, endorphins, and enkephalins that act by blocking substance P and other excitatory neurotransmitters activity on the primary afferent fibers (Berry *et al*., 2001).

D.) Perception:

The last step is perception which involves nociceptive processes as well as physiologic and emotional responses. It contributes to the sensation that is ultimately experienced by the person. Thus, the treatment that includes drug therapy to alter the nociceptive and physiologic response, in addition to the cognitive-behavioral strategies such as distraction, relaxation, and imagination (to alter the psychological response), may be effective when used together compared to when it is used alone. Most of the analgesic drugs inhibit prostaglandins synthesis in the periphery (Vadivelu *et al.*, 2009).

Antimicrobial study

Infectious diseases account for a very large proportion of diseases and the microorganisms are found to be responsible for a variety of infectious diseases. The frequency of life-threatening infections caused by pathogenic microorganisms has increased worldwide and is becoming an important cause of morbidity and mortality in immunocompromised patients in developing countries (Sofowara, 1982). The increasing prevalence of multi-drug resistant strains of bacteria and the recent appearance of strains with reduced susceptibility to antibiotics raised the spectrum of untreatable diseases and adds urgency to search for new infection fighting strategies (Cowan, 1999; Fransworth and Soejarto, 1991). Nature has been a source of medicinal agents for thousands of years and plant derived substances have recently become of great interest owing to their versatile applications (Baris *et al*., 2006). Plants offer a considerably greater chemical diversity than microorganisms. With advancement in technology and analytical chemistry, many compounds have been discovered from natural compounds and among them 50-60% are produced by plants (Berdy, 2005).

Antimicrobial Resistance and the Role of Plants

Resistance to antimicrobials is a natural biological phenomenon that can be accelerated by a variety of factors, including human practices. The past few decades have seen an alarming increase in the prevalence of antibiotic resistant microorganisms (Livermore, 2009). Bacteria are the most important pathogens causing severe infectious diseases including diarrhoea, tuberculosis, respiratory tract infections, sexually transmitted diseases etc. and contributing to infection related deaths (WHO, 2002). Over the last few decades, MRSA (Methicillin-resistant *Staphylococcus aureus*) strains have emerged as serious pathogens. These strains are often resistant to several antibiotic classes and are major cause of serious hospital and community acquired infections (Fang *et al*., 2004). India is well known historically as a land of spices and aromatic plants, and continues to be one of the leading producers of medicinal plants in the world (Prajapati *et al*., 2005). Herbal medicine forms the basis of treatment and cure for various diseases in traditional methods practiced such as Ayurveda, Unani, Siddha, Yoga, Homeopathy and Naturopathy. These systems aim at holistic management of health and disease (Cowan, 1999).

Plants as a Source of Antimicrobial Agents

Plants are rich in a variety of secondary metabolites such as tannins, terpenoids, alkaloids, flavonoids, phenols, steroids, glycosides and volatile oils that serve as natural plant defence mechanisms against

invasion by microorganisms, insects, and herbivores or for combating infectious or parasitic agents or generated in response to stress conditions (Cowan, 1999). Plant secondary metabolites possess a wide range of uses such as in food, flavours, poisons, perfumes, and scented oils in aromatherapy, industrial products such as dyes, rubber and oil. Traditionally, a number of herbs are recommended for various ailments and reported for their carminative, stomachic, antiinflammatory, antioxidant, antidiabetic, anticancer, antihypoglycemic, anti-hypertensive, antispasmodic, gastric acid suppressive, liver protective actions and anthelmintic activity (Egaule and Giday, 2009). Numerous studies have reported that medicinal plants produce a large number of secondary metabolites with antimicrobial effects on pathogens (Obagwu and Korsten, 2003).

Eugenia jambolana have promising therapeutic value with its various phytoconstituents such as tannins, alkaloids, steroids, flavanoids, terpenoids,fatty acids, phenols, minerals, carbohydrate and vitamins. In a study, the antimicrobial activity of *E. jambolana* leaves extract was done against clinical isolates by using well diffusion method. The different extracts showed inhibitory activity against clinical isolates of gram negative bacteria such as *Salmonella typhi* , *Shigella dysentriae*, *Kelbisiella pneumonia*, *Pseudomonas aeruginosa*, *Ecoli*, and gram positive bacteria such as *Bacillus subtilis*, *Staphylococcus aureus* (Jetthu *et al.*, 2011; Parkash *et al.*, 2011).

Pharmacological activities

The several parts of *E. jambolana* such as seed and pulp have a long standing history in the cure of various diseases as listed below:

Table 2: Various pharmacological properties of *E. jambolana*.

Sr. No.	Pharmacological properties	Uses	References
1.	Antiviral activity	Aqueous extract of the Jamun leaves were effective in inhibiting the replication of the buffalo-pox virus and goat-pox virus.	Bhanuprakash *et al.*, 2007
		Experiments have shown that the aqueous and methanolic extracts of the bark inhibited the HIV type 1 protease activity bymore than 70% at a concentration of 0.2 mg/mL.	Bhanuprakash *et al.*, 2008. Kusumoto *et al.*, 1995
2.	Anti-inflammatory activity	Ethanolic extract of the *E. jambolana* bark possess anti-inflammatory effects in both acute (carrageenan, kaolin carrageenin, and formaldehyde-induced) and chronic (cotton pellet granuloma) models in rats.	Muruganandan *et al.*, 2001.
		The chloroform fraction of the seed inhibited the carrageenin, kaolin and other inflammatory mediator-induced edema in rats.	Chaudhuri, Pal, Gomes, & Bhattacharya, 1990.

		The ethyl acetate and methanol extracts of seeds (200 and 400 mg/kg orally) are also reported to possess anti-inflammatory activities in the carrageenan induced paw edema in Wistar rats.	Kumar *et al.,* 2008
		The bark extract was effective in inhibiting the histamine, 5-HT and PGE_2-induced rat paw edema.	Muruganandan *et al.,* 2002
3.	Gastroprotective effects	Tannins isolated from Jamun were effective against the HCl/ethanol-induced gastric ulceration in rats.	Ramirez and Roa, 2003.
		Fruits of *E. jambolana* have shown to be effective in preventing ulcerations in both normal and streptozotocin-induced diabetic rats.	Chaturvedi *et al.,* 2009a, 2009b, 2007.
4.	Hepato-protective effects	Pulp extract *E. jambolana* was effective in preventing paracetamol-induced hepatotoxicity in rats.	Das and Sarma, 2009.
		Aqueous extract of the *E. jambolana* leaf and methanolic extract of the seed were effective against CCl_4-induced hepatotoxicity in rats.	Moresco *et al.,* 2007; Sisodia and Bhatnagar, 2009
		Treating hepatocytes with the extract (50 to 500 ppm) suppressed the CCl_4-induced release of LDH, decreased the lipid peroxidation, reversed the toxicant-induced changes in cellular glutathione level and increased the activity of the antioxidant enzyme GPx.	Veigas *et al.,* 2008
5.	Anti-diabetic activity and inhibition of lipid peroxidation	Jamun seeds are an important constitute in many of the polyherbal antidiabetic formulations in the Ayurveda, Siddha, Unani, Srilankan and Homeopathy.	Helmstadter, 2007; Helmstadter, 2008' Sharma *et al.,* 2009; Gohil *et al.,* 2010
		Jamun has been thoroughly investigated for its antidiabetic effects and the seed, pulp and bark have been found to have effective antidiabetic action, while the leaves of *E. jambolana* was ineffective. The seed *E. jambolana* is the most studied	Saravanan and Leelavinothan, 2006; Saravanan and Pari, 2007; Sharma *et al.,* 2006; Pepato *et al.,* 2005;Pepato *et al.,* 2001; Achrekar *et al.,*

		and the effective in causing anti-hyperglycemic effects in different models of study.	1991; Panda *et al*., 2009; Rathi *et al*., 2002; Ravi *et al*., 2005, 2004a, 2004b, 2004c, 2004d.
		Jamun seeds prevent the diabetes-induced secondary complications like nephropathy.	Sharma *et al*., 2008b; Sharma, Viswanath *et al*., 2008a; Sharma *et al*., 2003.
		Human studies have shown that *E. jambolana* possess promising anti-hyperglycemic effects. The mycaminose (50 mg/kg), isolated from the seeds. Jamun also possess anti-hyperglycemic effects in the streptozotocin-induced diabetes in rats. Feeding Jamun has also been shown to enhance the levels of serum insulin levels in both normoglycemic and diabetic rats stimulate synthesis of insulin from the residual beta cells and also inhibits the insulinase in the liver and kidney and to trigger the development of insulin positive cells from the epithelial cells of the pancreatic duct.	Sridhar *et al*., 2005; Sundaram *et al*., 2009; Villasenor and Lamadrid, 2006; Kar *et al*., 2003; Suganthi *et al*., 2007; Vikrant *et al*.,2001. Srivastava *et al*.,1983; Kohli and Singh, 1993; Sahana *et al*., 2010. Kumar *et al*., 2008. Grover *et al*., 2000
		In-vitro studies have also shown that Jamun seed possess inhibitory effect on both pancreatic amylase and α-amylase.	Helmstädter, 2008; Schossler *et al*., 2004; Ponnusamy *et al*., 2010; Karthic *et al*., 2008.
		The Jamun seed extract fraction is also reported to activate glucose transport in phosphatidylinositol 3′kinase-dependent fashion in a cell culture model .	Anadharajan *et al*., 2006; Anadharajan *et al*., 2006; Rau *et al*. 2006; Khan *et al*., 2005.
		Jamun extract upregulated the glucose transporter Glut-4 and activated the peroxisome proliferator-activated receptor.	Arayne *et al*., 2007; Prince *et al*., 2004, 1998; Ravi *et al*. 2004c; Stanely Mainzen Prince *et al*., 2003.

		Both methanolic and aqueous extracts inhibited glucose utilization, with the results being better in the neutral and basic than in the acidic media.	Sultana *et al.,* 2007; Prince, Menon and Pari, 1998.
6.	Hypolipidaemic effect	Feeding ethanolic extract of the seeds of *E. jambolana* to alloxon-induced, seed kernel (100 mg/kg body weight) to streptozotocin-induced and flavonoid enriched extract from seeds to diabetic rats caused hypolipidemic effect.	Sharma *et al.,* 2003 Ravi *et al*., 2005 Sharma & Viswanath *et al.*, 2008a; Sharma & Balomajumder and Roy, 2008b.
7.	Cardioprotective effect	The methanolic extract of the *E. jambolana* seeds is reported to possess cardioprotective effects in the isoproterenol-induced Myocardial Infarction model in rats.	Mastan *et al*., 2009
8.	Antidiarrhoeal effect	The ethanolic extract of the *E. jambolana* tree bark was effective in preventing castor oil-induced diarrhea, PGE_2-induced enteropooling and to reduce gastrointestinal motility.	Mukherjee *et al*., 1998.
9.	Anti-fertility effect	Chronic administration of oleanolic acid, a constituent of the *E. jambolana* flowers shown to possess antifertility activities in the male albino rats.	Rajasekaran *et al*., 1988
10.	Anti-allergic effect	Aqueous extract of *E. jambolana* leaf shown to possess antiallergic effects in mice.	Brito *et al.,* 2007.
11.	Anti-pyretic effect	*E. jambolana* possess significant anti-pyretic action against the yeast-induced pyrexia in mice.	Chaudhuri *et al.,* 1990
12.	Anti-neoplastic, Radio-protective and chemo-protective effects	*E. jambolana* extract induced cytotoxic effects against the human cervical cancer cells the HeLa and SiHa. The *E. jambolana* fruit extract caused selective cytotoxity to the MCF-7aro and MDA-MB-231 but not to the normal/ nontumorigenic MCF-10A cells. Ellagitannins obtained from *E. jambolana* inhibited Wnt signaling in a human 293 T cell line. The hydroethanolic extract of the *E. jambolana* seeds prevented the DMBA-	Barh and Viswanathan, 2008. Li & Adams *et al.,* 2009; Li, Zhang and Seeram, 2009. Sharma *et al*., 2010. Parmar, Sharma, Verma and Goyal,

		induced croton oil promoted skin and benz- a pyrene-induced gastric carcinogenesis in mice. Administration of the hydroalcoholic extract of the *E. jambolana* seeds and the dichloromethane extract of *E. jambolana* leaves possess radioprotective effects. The dichloromethane extract of *E. jambolana* leaves also afforded enteroprotective effects against the radiation-induced damage to the GIT in mice.	2010; Parmar, Sharma, Verma, Sharma *et al.,* 2010b; Goyal *et al.,* 2010. Jagetia and Baliga, 2003; Jagetia *et al.,* 2005; Jagetia and Baliga, 2008.
13.	Anti-clastogenic effect	The methanol:dichloromethane extract *of E. jambolana* reduces the radiation-induced DNA damage in the cultured human peripheral blood lymphocytes. Aqueous and ethanolic extracts of *E. jambolana* seeds reduced the hydroxyl radical-induced strand breaks in pBR322 DNA in vitro. Aqueous extract of *E. jambolana* also reduced the genotoxic of the carcinogens urethane and DMBA in mice.	Jagetia and Baliga, 2002. Arun *et al*., 2010. Arun *et al.,* 2010.
14.	CNS depressant activity	Administering chloroform extract of *E. jambolana* seeds caused CNS depressant action. The ethyl acetate and methanolic extract of the *E. jambolana* seed also shown to modulate CNS activity.	Chakraborty *et al.,* 1986. Kumar *et al.,* 2007.
15.	Antioxidant activity	The antioxidant effects of the ethanolic extract of fruit pulp, kernel and seed coat were evaluated in various in vitro assays (DPPH•, OH• and O2•−) with gallic acid, quercetin and trolox. The methanol-formic acid (9:1) extract of the fruit, the hydroethanolic extract of the seed, methanolic extract of the stem, anthocyanin-rich fruit peel extract, the methanolic extract of the leaves and the hydrolysable and condensed tannins	Alia *et al.,* 2008; Rufino *et al.,* 2010; Sanchez-Moreno, Larrauri, & Saura-Calixto, 1999; Benherlal and Arumughan, 2007 Reynertson *et al*., 2008; Raquibul-Hasan *et al*., 2009; Kshirsagar & Upadhyay, 2009; Veigas *et al.,* 2007;

		present in the fruits.	Nahar *et al.*, 2009 Zhang & Lin., 2009
		The organic extract of the leaves (methanol: dichloromethane extract) as well as the hydroethanolic extract of the seeds are reported to be a scavenger of nitric oxide *in-vitro*.	Jagetia & Baliga, 2004
		The methanolic extract was subjected to fractionation with water, ethyl acetate, chloroform and n-hexane, and studied their free radical scavenging effects in the DPPH and FRAP assays.	Ruan *et al.*,2008
		Studies have shown that the fruit skin of Jamun possess antioxidant effects as confirmed by results from the hydroxyl radical-scavenging assay, superoxide radical-scavenging and DPPH radical-scavenging assay in vitro.	Banerjee *et al.,* 2005
		The anthocyanin-rich fruit peel extract is also observed to be effective as a reducing agent. Recently observed that the hydromethanolic extract of the Jamun seed was effective in scavenging (90.6%) free radicals as evaluated in the auto-oxidation of β-carotene and linoleic acid assays.	Veigas *et al.,* 2007; Bajpai *et al.,* 2005.
16.	Anti-bacterial activity	The hydroalcoholic extract of *E. jambolana* leaves is shown to possess antibacterial effects against *Enterococcus faecalis, Escherichia coli, Kocuria rhizophila, Neisseria gonorrhoeae, Pseudomonas aeruginosa, Shigella flexneri, Staphylococcus aureus* and the multi-resistant *Klebsiella pneumonia.*	De Oliveira *et al.,* 2007.
		The petroleum ether, methanolic and ethyl acetate extract of the *E. jambolana* leaves shown to possess antibacterial effects on *Bacillus subtilis, S. aureus, P. aeruginosa, Salmonella typhimurium and Enterobacter aerogenes*. Methanolic extract was better than other extracts and more effective on gram positive organisms.	Kaneria *et al.,* 2009

		The aqueous extract of *E. jambolana* leaves has shown to be effective against the clinical isolates of *Citrobacter* sp., *E. coli, Klebsiella* sp., *Proteus mirabilis, P. aeruginosa, Salmonella typhi, S. typhimurium, Salmonella paratyphi A, Salmonella paratyphi B, Shigella boydii, Shigella flexneri, Shigella sonnei, S. aureus and Streptococcus faecalis.*	Satish *et al.,* 2008
		The methanolic and ethyl acetate extracts of *E. jambolana* seed has shown to be effective against *Bacillus cerus, B. subtalis, B. megateriun, Steptococcus beta haemolyticus, S. aureus, Shigella dysenteriae, S. Shiga, S. boydii, S. flexneriae, S. sonnei, E. coli, S. typhi B, S. typhi B-56 and Klebsiella species.*	Bhuiyan *et al.,* 1996.
		The methanolic extract of *E. jambolana* seed is effective against *Vibrio cholerae* (serotypes O1, O139, and non-O1, non-O139), *K. pneumoniae, A. hydrophila, Enterotoxigenic E. coli, P. aeruginosa and B. subtilis,* but are ineffective against *Enterohaemorrhagic E.coli* strain VT3.	Acharyya *et al.,* 2009
		The aqueous, ethanolic and acetone extracts of the *E. jambolana* bark was studied for its antibacterial effects on twelve strains of *V. cholerae*. The ethanolic extract was the most effective while the aqueous and acetone extracts were less effective.	Sharma *et al.,* 2009.
		The aqueous, methanolic and hydromethanolic extracts *E. jambolana* are also effective against the cariogenic bacteria, *Streptococcus mutans* and to inhibit/suppress the plaque formation *in-vitro.*	Namba *et al*., 1985.
		The essential oil of *E. jambolana* has been shown to possess antibacterial effects on *Basillus sphaericus, B. subtilis, S. aureus, E. coli, P. aeruginosa* and *S. typhimurium.* The effect was profound for *S.*	Shafi *et al.,* 2002.

		typhimurium and least for *E. coli*.	
17.	Anti-fungal activity	The hydroalcoholic extract of *E. jambolana* leaf is shown to possess antifungal effects against *Candida albicans* and *C. krusei*.	Chandrasekaran and Venkatesalu, 2004
		The aqueous and methanolic extracts *E. jambolana* inhibited growth of dermatophytic fungi *C. albicans, T. rubrum, T. mentagrophytes and M. Gypseum.*	Jabeen and Javaid, 2010
		The aqueous, ethanol and n-hexane extracts of *E. jambolana* from the leaves, fruit, root-bark and stem-bark possess growth inhibitory effects on *Ascochyta rabiei*, the causative agent of blight disease in chickpea (*Cicer arietinum* L.). The aqueous extracts of all the four plant parts showed significant antifungal activity.	Satish *et al.*, 2008
		The petroleum ether, benzene, chloroform, methanol, ethanol and aqueous extracts of the *E. jambolana* leaf were studied on *A. candidus, A. columnaris, A. flavipes, A. flavus, A. fumigatus, A. niger, A. ochraceus and A. tamari.* The methanolic extract was more effective than the other extracts.	De Olieviera *et al.*, 2007

Discussion

There are extensive and diverse natural resources that are available for production of useful products such as antibiotics (Fox and Howlell, 2008). The bacterial and yeast cultures used in the present study were responsible for causing gastrointestinal tract infections, respiratory and skin infections. The worldwide spread of Methicillin-resistant *S. aureus* (MRSA) has been observed (Talbot *et al*., 2006). Multidrug resistant pathogens, especially bacteria, emerged as a major therapeutic challenge complicating the antibiotic therapy regime. It prompted the discovery and development of new antibiotics to combat difficult-to-treat infections caused by such pathogens (Livermore, 2009). This situation coupled with the undesirable side effects of certain antibiotics and the emergence of previously unknown infections leading to the failure of chemotherapeutics has necessitated a search for new antimicrobial and chemotherapeutic agents that combine antimicrobial efficacy with low toxicity and minimum environmental impact (Song, 2008). The present review was focused on the seeds of *E. jambolana* extracts for the pharmacognostic studies. The extracts of *E. jambolana* which are best effective in analgesic as well as antimicrobial activities are in conjunction with the phytochemical constituents present in the seeds of the plant. Thus, the phytochemical screening of *E.*

jambolana extracts revealed that the petroleum ether extract contains terpenoids, chloroform extract contains alkaloids and tannins, methanol extract contains flavonoids, tannins, glycosides, saponins and alkaloids were present in aqueous extract. Many authors have reported that the phenolic compounds such as flavonoids, tannins, cyanins, triterpenoids and other phenolic compounds possess multiple biological activities such as antinociceptive and inhibitory action on arachidonic acid metabolism (Kumar *et al.,* 2008; Muruganandan, 2001). The study revealed petroleum ether and methanol to be the best solvent to isolate the compound responsible for antimicrobial activity while aqueous and chloroform extract was resiatant to all the test organisms. Mashhadian and Rakshandeh (2005) according to which methanol extract gave better results than aqueous extracts which was ineffective. *Staphylococcus aureus*, one of the major bacterial pathogens of man, causing a variety of diseases and also the most common cause of nosocomial infections (Prakash *et al*., 2007) showed the better sensitivity to plant extracts in comparison to the standard antibiotics.

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