Current Pharma Research
ISSN-2230-7842
CODEN-CPRUE6
www.jcpronline.in/

Review Article

Barleria Prionitis: It's Pharmacognosy, Phytochemicals and Its Potential Beneficial Effects in Common Oro-Dental Diseases.

Sufiyan Ahmad[*,1], Md. Rageeb Md. Usman[2], Bharat V. Jain[2], Mohammed Zuber Shaikh[3]

[1]Department of Pharmacognosy, Gangamai College of Pharmacy, Nagaon, Dist. Dhule, Maharashtra, India.

[2]Department of Pharmacognosy and Pharmaceutics, Smt. S. S. Patil College of Pharmacy, Chopda, Maharashtra, India.

[3]Department of Zoology, Senior Science College, Akkalkuwa, India.

Received 12 April 2020; received in revised form 08 May 2020; accepted 13 May 2020

***Corresponding author E-mail address:** *rageebshaikh@gmail.com*

ABSTRACT
Natural products are a rich source of chemical constituents with wide structural diversity, along with tremendous therapeutic potential. So that the medicine derived from natural sources such as plants, microorganisms, marine, etc. are the endowments of nature for the endurance of life. Barleria prionitis is a famous perennial plant commonly known as porcupine flower or Vajradanti. It is a shrub with yellow flowers and two flat seeds shielded with matted hairs, inhabit most parts of India. Various parts of the plant such as leaves, roots, aerial parts, flowers, and stems are used in the traditional system of medicine. Conventionally, various infusions are prepared using the plant parts and utilized for the treatment of different kinds of diseases. It is one of the vital ingredients of many herbal teeth formulations. From the pharmacological point, the plant has been effectively screened for antibacterial, antifungal, antiviral, anti-inflammatory, antifertility, antioxidant, anticancer, and anticataract activities. Compounds such as tannins, saponins, glycosides, phenolic acids, phytosterols, and terpenes have been identified in the plant. The plant contains some specific compounds such as barlenoside, barlerine, acetylbarlerine, and balarenone and some common secondary metabolites such as lupeol, β-sitosterol, vanillic acid, and syringic acid. This review gives insight into the botany, ethnomedicinal uses, phytochemistry, pharmacological activities, clinical study, quality control, and formulations of Barleria prionitis.

KEYWORDS
Barleria prionitis, Procupine flower, Vajradanti, ethnomedicinal uses, iridoids, phytochemistry, formulations.

1. INTRODUCTION

1.1. Dental Caries

Dental caries is a localized and progressive decay of the teeth. Not only does it cause many people to experience a great deal of pain, it leads to continuous discomfort through inconvenient treatment. WHO's report on the Global Problem of Oral Diseases, notes that oral diseases such as dental caries (tooth decay), periodontitis (gum disease) and oral and pharyngeal cancers are global health problem in both the industrialized and the developing countries, especially among poorer communities. Dental caries is a major oral affliction in developing countries, affecting 60-90% of the school children and the vast majority of adults. An estimated five billion people worldwide have experienced dental caries [1]. Figure 1 highlights the dental caries experience among 12-year-old children in the six WHO regions in the year 2000, based on the DMFT (Decayed, Missing and Filled Teeth) Index, which measures the lifetime experience of dental caries in permanent dentition. In developing countries like India, the rate of dental caries is rising and since more than 80% of the world's children live in these countries, dental caries is considered to be a major public health problem [2].

1.2. How dental caries are caused?

Dental caries is a multifactoral infectious disease in which the active agent or agents are members of the indigenous oral flora (Figure 2). Oral cavity harbors a rich and diverse microbial flora because of its ideal humidity and temperature, the frequent passage through it of most nutrients needed by many microbial species and presence of several ecological niche. The presence of a myriad of microorganisms is a natural part of proper oral health. Oral microbes can adhere to surfaces throughout the oral cavity. These include the tongue, epithelial cells lining roof of the mouth and the cheeks, and enamel of the teeth [3].

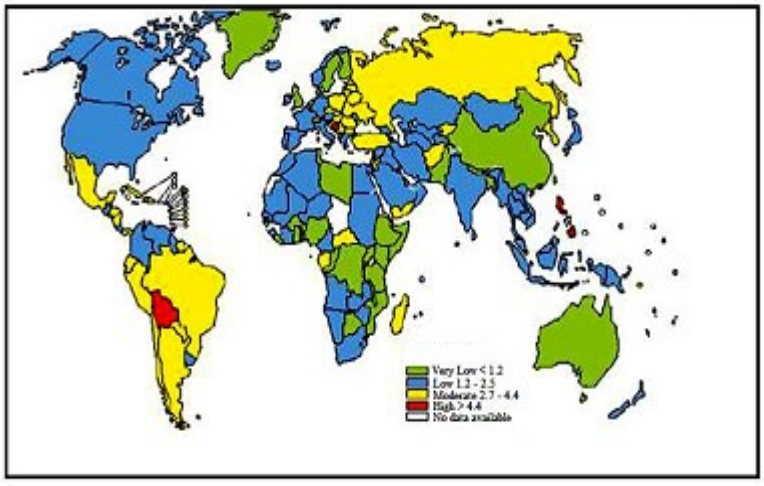


Fig. 1. Dental caries levels (DMFT) of 12-year-olds worldwide WHO.

1.3. Microbial and host ecology

Under the conditions in which the human-oral microflora relationship evolved, the bacteria that inhabit the human mouth appear to have a commensal or even mutualistic relationship with their human host and with each other. The mouth can be considered an ideal environment for the growth of microorganisms, since it is warm and moist and has a constant influx of nutrients through saliva and food intake. In fact, it has been calculated that there are as many as 4×10^{10} organisms in each gram of plaque removed from the teeth [4]. These organisms consist of, on an average, more than 400 species that live together through the exploitation of very specific ecological niches. For example, Lactobacilli are known to favour the dorsum of the tongue, while Streptococcus mutans requires a solid, non-shedding surface for colonization, as demonstrated by the rapid appearance of S. mutans in the mouth of toothless infants when obturators are inserted to fix cleft palates. This complex relationship even consists of bacteria whose presence is contingent on other "pioneer" bacterial species. It has even been demonstrated that certain oral microorganisms can cooperate in a mutualistic manner for a common benefit, as when species collaborate by using different species-specific enzymes to break down complex host molecules that could not be metabolized by a single species.

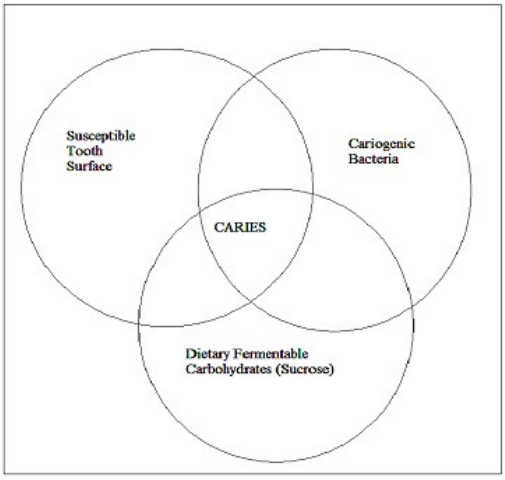


Fig. 2. Dental caries is a multifactoral infectious disease.

The ecology of the mouth, however, does not just involve interactions among microorganisms. In fact, the host plays a large role in maintaining a uniform ecosystem, especially through the saliva. Saliva is a complex mineral- and protein-rich solution that delivers nutrients to the many bacterial species within the mouth while also protecting host surfaces. During mastication, increased saliva flow prevents changes in oral pH, because the buffer bicarbonate is present in saliva and acts as an acid sink at a time when acidic products are being introduced into the mouth. Urea and the peptide sialin are both also present in low concentrations in saliva and produce ammonia when hydrolyzed, a basic product capable of raising pH. This basicity and buffering counteracts the lactic acid produced by anaerobic bacteria in the mouth during the fermentation that occurs when nutrients are introduced,

offsetting decay of the teeth caused by this acid. Saliva also contains glycoproteins that are known to be antibacterial, such as lysozyme and lactoperoxidase. These compounds act independently of the host's immune system, and are able to destroy invasive bacteria without harming the ecological balance of the oral cavity, since indigenous bacteria have evolved resistance. A remarkable example of the balanced relationship between saliva and oral microbiota is the fact that saliva is actually supersaturated with calcium and phospate ions, which precipitate to form hydroxyapatite and remineralize the teeth. This supersaturated solution should theoretically result in uncontrollable tooth growth as more and more calcium phosphate precipitates onto the teeth. However, proteins containing proline and a peptide called statherin, both of which are present in saliva, have been shown to slow the rate of precipitation of these ions to a rate which perfectly matches the rate of decay induced by bacteria during normal lactic acid formation. Under these conditions, teeth should be caries-free while the mouth remains colonized. The extensive decay and rampant levels of S. mutans in patients suffering from xerostomia, or reduced saliva flow, is a striking example of the role of saliva in caries prevention. In fact, patients undergoing radiation for head and neck cancers are often used as models for the progression of decay, since severe xerostomia is an almost universal side effect of such treatment [5-6].

1.4. Pathogenic Bacteria

Historically, cavities were attributed to a general overgrowth of oral bacteria, termed the “non-specific plaque hypothesis.” However, this was disproved by Keyes (1960), who compared the bacterial make-up of caries-active and caries-inactive hamsters and found much higher proportions of a group of bacteria termed the “mutans streptococci” in the cariogenic hamsters. He further showed that hamsters without caries did not develop them until exposed to caries-active hamsters or their faeces. The mutans streptococci could be isolated from these newly caries-active hamsters, and cultures of the bacteria would also cause caries in caries-free hamsters. Keyes' hamster experiments showed that these bacteria fulfilled Koch's postulates for infectious disease and led to the adoption of the “specific plaque hypothesis,” which states that only certain bacterial species are responsible for cariogenic behavior (Gibbons 2005). This breakthrough made researchers eager to discover which bacterial species were responsible for caries formation. Caries are formed when the rate of decay of the teeth caused by the lactic acid produced by anaerobic bacteria exceeds the rate of repair initiated by the phosphate and calcium ions in saliva. Lactic acid production surges when sucrose is introduced into the mouth during meals or snacks, resulting in an overall drop in oral pH. Thusly, if acidity is a prerequisite for caries formation, then only species that thrive in an acidic environment, known as acidophilic species, can play a role in producing them. In fact, when cultures simulating a community of oral bacteria were pulsed with glucose to produce a constant pH lower than 5, the acidophilic species Lactobacillus casei, Veilonella dispar, and especially Streptococcus mutans were able to dominate niches previously occupied by other, avirulent species, and became irreversibly over-represented in the population [7].

1.5. What are periodontal diseases?

The word "periodontal" literally means "around the tooth."Periodontal diseases are bacterial gum infections that destroy the gums and supporting bone that hold your teeth in your mouth. Periodontal diseases can affect one tooth or many teeth. The main cause of periodontal diseases is bacterial plaque, a sticky, colorless film that constantly forms on your teeth. If the plaque is not removed, it can turn into a hard substance called calculus or tartar in less than two days. Tartar is so hard it can only be removed by an oral health professional, such as a dentist or dental hygienist. The bacteria in plaque infect the gums, and release poisons that cause redness and inflammation (irritation). The inflammation and the poisons themselves cause destruction of the tissues that support the teeth, including the bone. When this happens, the gums separate microscopically from the teeth, forming pockets that fill with even more plaque causing even more infection. Periodontal diseases are multi-factorial. This means that there is not just one cause of periodontal diseases but rather multiple factors that can affect the health of your gums.

Tobacco use significantly increases the risk of developing periodontal diseases and can negatively affect treatment.

Hormonal changes during pregnancy, puberty and menopause can cause the gums to become red, tender and bleed easily.

Genetics and family history of periodontal diseases indicate a greater likelihood of developing these diseases.

Stress can make it more difficult for the body to fight off infection, including periodontal diseases.

Some **Medications** such as oral contraceptives, antidepressants and certain heart medicine, can affect oral health.

Destructive habits such as improper oral hygiene technique, oral piercing, drug or alcohol abuse can affect periodontal health.

Poor nutrition can make it harder for the body to fight off infection.

Systemic diseases that interfere with the body's immune system may worsen the condition of the gums and supporting bone [8-10].

1.6. Types of periodontal diseases

Gingivitis: As the mildest form of the periodontal diseases, gingivitis causes the gums to become red, swollen, and bleed easily. There is usually no discomfort at this stage.

Chronic Periodontitis: Chronic periodontitis is a condition resulting in inflammation within the soft tissues surrounding the teeth causing progressive attachment and bone loss (see Figures 3). It is diagnosed by bone loss on a dental X-ray, the formation of gum pockets and/or receding gums. It is most common in adults, but can occur at any age.

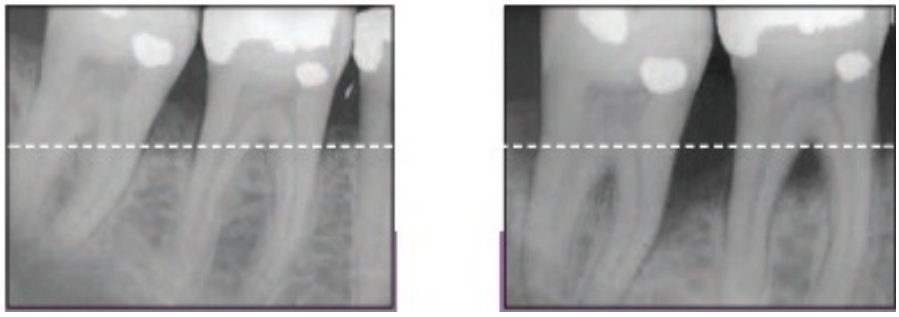


Fig. 3. Bone loss due to chronic periodontitis

Aggressive Periodontitis: This form occurs in patients who are otherwise in good health. Common features include rapid attachment loss and bone destruction. There are two forms of aggressive periodontitis:

Localized Aggressive Periodontitis: Most often occurs near puberty and usually involves attachment loss around first molars and/or front teeth but may involve one or two additional teeth.

Generalized Aggressive Periodontitis: Usually, but not always affects people under 30 years of age. It involves attachment loss on at least three permanent teeth in addition to first molars and incisors. Periodontitis as a Manifestation of Systemic Disease As the name indicates, this form is associated with one of several systemic diseases that are related to periodontitis, such as diabetes.

Necrotizing Periodontal Diseases: These types of periodontal diseases cause ulcers in the gums between the teeth and are most commonly observed in individuals with certain conditions including, but not limited to, HIV infection, malnutrition and immuno suppression. Stress, smoking, and poor oral hygiene sometimes can contribute to this problem.

1.7. What are the signs of periodontal diseases?

Periodontal diseases are often silent, meaning that symptoms may not materialize until significant bone loss has occurred. Some people may have periodontitis and not experience any symptoms and be unaware that they have disease. Common symptoms and signs of periodontal diseases include:

- Red, swollen or tender gums
- Bleeding while brushing or flossing
- Gums pulling away from the teeth
- Making teeth appear longer
- Loose or separating teeth
- Pus between the gum and tooth
- Persistent bad breath
- A change in the way your teeth
- Fit together when you bite
- A change in the fit of partial dentures

If you notice any of these symptoms, you should see a periodontist for a complete periodontal examination. A periodontist is a dentist who specializes in the prevention, diagnosis and treatment of tissues surrounding the teeth. In addition, periodontists are experts in the placement and maintenance of dental implants. During a periodontal examination, the periodontist will gently place a small measuring instrument called a periodontal probe in the pocket between the teeth and gums to measure pocket depths and help make a diagnosis. Probing depths measuring 1-3mm are usually considered healthy. Four to 5mm may indicate mild periodontitis, 5-6mm suggest moderate periodontitis, and 7mm or greater may indicate severe periodontitis. In addition to probing depth measurements, X-rays may be taken to evaluate the health of the bone supporting the teeth Figure 4.

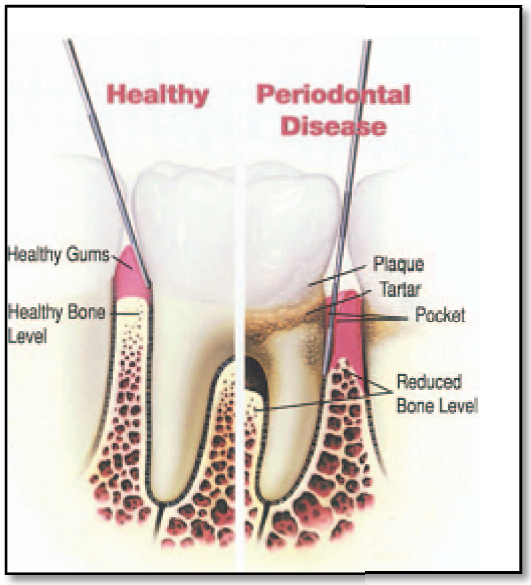


Fig. 4. Complete periodontal examination.

1.8. How are periodontal diseases treated?

Once your periodontal health has been evaluated, your periodontist will work with you to determine the best treatment options to control your disease and bring you back to health. Treatment can vary depending on how far the disease has progressed. If diagnosed and treated in the early stages, simple non-surgical periodontal therapy may be sufficient. If periodontitis has advanced to the point where the periodontal pockets are deep and significant amounts of bone are lost, surgical therapy may be necessary. Once periodontitis has been controlled, patients will require ongoing periodontal maintenance procedures to sustain health.

This ongoing phase of treatment will allow your periodontist to assess your periodontal health and make sure that your infection stays under control or remains eliminated. During these re-evaluation appointments, your mouth will be examined, new calculus and plaque will be removed and, if necessary, your teeth will be polished and your bite will be checked. Periodontal

diseases are chronic diseases, just like diabetes. Without careful, ongoing treatment, periodontal diseases can and often do recur.

1.9. How can the periodontal diseases be prevented?

Good oral hygiene and professional care are the keys to keeping your teeth for a lifetime. The best way to prevent periodontal diseases and tooth decay is to remove the bacterial plaque by thorough brushing and flossing every day. Good oral hygiene habits will help keep the formation of dental tartar to a minimum. Regular dental visits that include a periodontal examination are also important to detect any changes in periodontal health and, if necessary, to remove hardened tartar in places that your toothbrush and floss may have missed. A professional cleaning (often called a prophylaxis) at least twice a year is recommended for patients with good periodontal health. If you have had any form of the periodontal diseases, you may need professional maintenance more frequently. Congratulations on taking the first step to achieving periodontal health! Preventing and/or controlling periodontal diseases is a worthwhile commitment that will keep you smiling for life [11-13].

1.10. Introduction of plant

Medicinal plants are used worldwide in management of healthcare problems since time immemorial and approximately 60-80% of the world's population still depending on the traditional medicines [14-19]. Currently, the global demand of herbal medicines is increasing rapidly because of their higher safety margin and low cost [20]. Medicinal plants are believed to be a potential source for the discovery of new drug candidates [21-24]. Numbers of active compound classes like alkaloids, terpens, flavonoids, glycosides, lignans, phenolics, saponins etc has been used in the modern system of medicines for their wide therapeutic activities [25-29].

Ayurveda, a traditional systems medicine in India, have major treatment globally [30]. B. prionitis Linn. (family: Acanthaceae) is well-known medicinal plant in ayurvedic system of medicine in India. The whole plant, root, leaves and bark of the plant occupy a significant place in the indigenous system of medicine of India for the treatment of various diseases like toothache, inflammations, boils, glandular swellings, catarrhal affections etc. [31-34]. In India it has several vernacular names like In English-yellow nail-dye plant, porcupine flower; Sanskrit-vajradanti, kurantaka, koranta; Hindi-kala bans, katsareya, piabansa; Bengali-kantajinti, peetjhanti; Gujarati-kantashila; Kannada-karunta, mullugorante; Malayalam-chemmulli, varelmutti; Marathi-kalsunda, kate koranti, kholeta, koranta, pivala-koranta; Odia-daskeranta; Tamil-kaattu kanagaambaram, semmulli and in Telugu-mullugorinta chettu. In Indian traditional systems of medicine (Ayurveda) it is known as sahachara, baana, kurantaka, kuranta, koranda, korandaka, shairiya and pita-saireyaka. In folk medicine it is known as piyaabaasaa, jhinti and katsaraiyaa Here, the attempt has been made to highlight its traditional uses, phytoconstituents, pharmacology and toxicity.

1.11. Distribution

It is commonly found in tropical Asia include India, Malesia, Pakistan, Philippines, Sri Lanka and in tropical Africa and Yemen. This plant is distributed throughout the hotter parts of India and commonly grown in gardens as a hedge plant. It is commonly found in the states of India

include Andaman and Nicobar Islands, Andhra Pradesh, Assam, Bihar, Chhattisgarh, Delhi, Diu and Daman, Goa, Gujarat, Jharkhand, Karnataka, Kerala, Laccadive and Maldiv Islands, Madhya Pradesh, Maharashtra, Orissa, Pudhucherry, Rajasthan, Tamil Nadu, Uttarakhand, Uttar Pradesh and West Bengal [35-36].

1.12. General Botanical Description

B. prionitis is a perennial, erect, bushy shrub grows up to 1-2 m high. They posses 2-4 sharp long axillary spines which about 11 mm long. The stems are terete, glabrous, much branched with cylindrical and tapering branchlet. Leaves are smooth, opposite, ovate-elliptic to obovate, acuminate, tapering to base, bristle-tipped and about 6-15 cm long and 4-6 cm wide. The petioles are about 0.5-3 cm long. The flowers are sessile, yellow in colour and often solitary in lower axils and spictate in the upper axils. Bracts are acute, linear-lanceolate, foliaceous, about 1-1.5 cm long and 0.2-0.8 cm wide with bristle tipped. The bracteoles are long, narrowly linear-lanceolate, spinous-tipped, about 1.4 cm long and 0.15 cm wide. The calyx is two partite. The outer calyx-lobes are mucronate, ovate-oblong and inner lobes are mucronate, linear-lanceolate. The outer lobes are 1.5 cm long and 0.4 cm wide while the inner lobes are 13 mm long and 2 mm wide. The corolla is bright, golden yellow in colour with pubescent outside and glabrous inside and about 1.5 cm long. It is somewhat bilipped and lobes are oval-oblong, rounded and entire. The stamens include 2 fertile stamens and 2 staminoid stamens. The fertile stamens are exerted beyond the corolla tube while the staminod stamens are very short. The filaments are hairy and about 2-2.5 cm long, glandular-pubescent and yellowish in colour. The yellow anthers are 3 mm long. The ovary is ovoid and sigma is long, linear, sticky and pinkish in colour. The fruit capsule is ovoid, 2 seeded and about 1.5-2 cm long and 0.6-0.8 cm wide. The seeds are oval-oblong, covered with silky copper-brown appressed hairs and measuring about 7.4-8.5x6-6.8 mm [37-38].

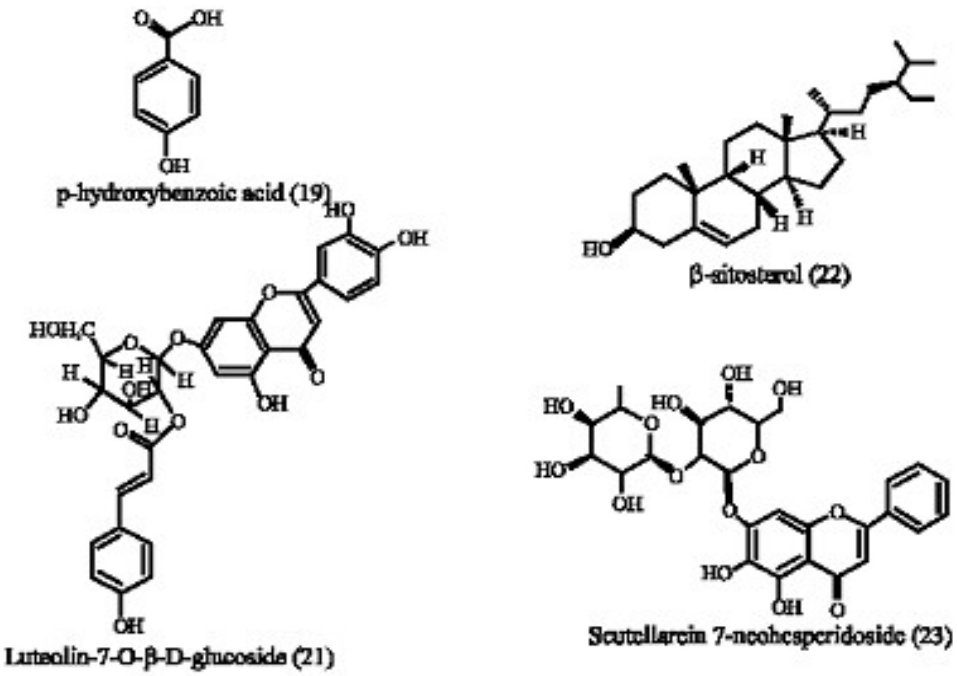
1.13 Use in traditional medicine

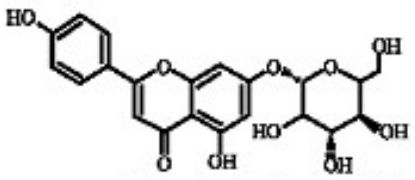
In indigenous system of medicine in India, the juice of B. prionitis leaves is used in stomach disorders, urinary affections, ulcer and fever. The leaf juice mixed with honey given to children in catarrhal affections and fever. Leaves are chewed to relieve from toothache. Some tribal communities are used leaves for the treatment of piles and reduce irritation. The leaf juice is applied externally in lacerated soles of feet and pimples. The dried stem bark is used as an expectorant in whooping cough and diaphoretic. The aerial parts of this plant are also used in inflammations and gastrointestinal disorders. The root paste is externally applied to disperse boils and glandular swellings. The flowers are used internally for the treatment of migraine, internal abscesses, oedema, haemoptysis, urethral discharges, seminal disorders and reduce obesity. The whole plant is also used in stiffness of limbs, enlargement of scrotum and sciatica. The whole plant, specifically the roots are used as diuretic and tonic. It is also used in urinary infection, jaundice, hepatic obstruction and dropsy. Ash of the whole plant with honey is given in bronchial asthma. The crude extract of this plant in oil is recommended in arresting the greying of hair, arthritis and gout. In South India, this plant is widely used in neurological disorders like paraplegia, sciatica, also in leprosy and other skin diseases. The plant formulation, available in

over the counter is prescribed in dysurea, rheumatic affections, internal abscesses, nervine disorders and in chronic sinusitis [39-40].

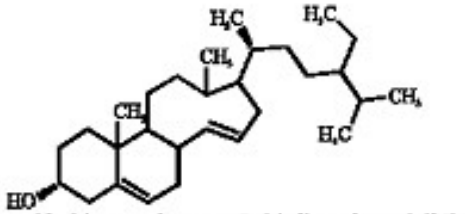
1.14. Phytochemistry

Preliminary phytochemical analysis of hydro-methanolic extract of B. prionitis whole plant indicated the presence of glycosides, saponins, flavonoids, steroids and tannins [41]. The leaves and flowering tops were reported to rich in potassium salts. Several phytochemicals viz., balarenone (1), pipataline (2), lupeol (3), prioniside A (4), prioniside B (5) and prioniside C (6) has been isolated from the ethanolic extract of B. prionitis [42-43]. Numbers of glycosides include barlerinoside (7), verbascoside (8), shanzhiside methyl ester (9), 6-O-trans-p-coumaroyl-8-O-acetylshanzhiside methyl ester (10), barlerin (11), acetylbarlerin (12), 7-methoxydiderroside (13), lupulinoside (14) has been also isolated from the aerial parts [44-46]. Two anthraquinones derivatives has been also identified in this plant and their structures were characterized as 1,8, dihydroxy-2,7-dimethyl 3, 6-dimethoxy anthraquinone and 1,3,6,8-tetra methoxy-2,7-dimethyl anthraquinone [47]. The leaves were reported to contain scutellarein (15), melilotic acid (16), syringic acid (17), vanillic acid (18), p-hydroxybenzoic acid (19), 6-hydroxyflavones (20). Beside these phytochemicals, luteolin-7-O-β-D-glucoside (21), β-sitosterol (22), scutellarein 7-neohesperidoside (23), apigenin 7-O-glucoside (24), 13, 14-seco-stigmasta-5, 14-diene-3-a-ol (25) were also reported to present in B. prionitis [48-50]. The structures of some phytochemicals are given in Fig. 5.

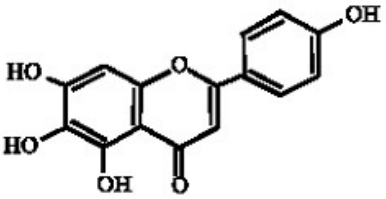




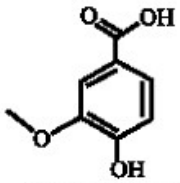
Apigenin 7-O-glucoside (24)



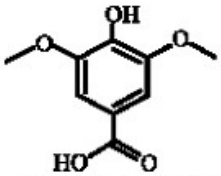
13, 14-seco-sigmasta-5, 14-diene-3-α-o1 (25)



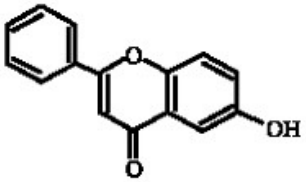
Scutellarein (15)



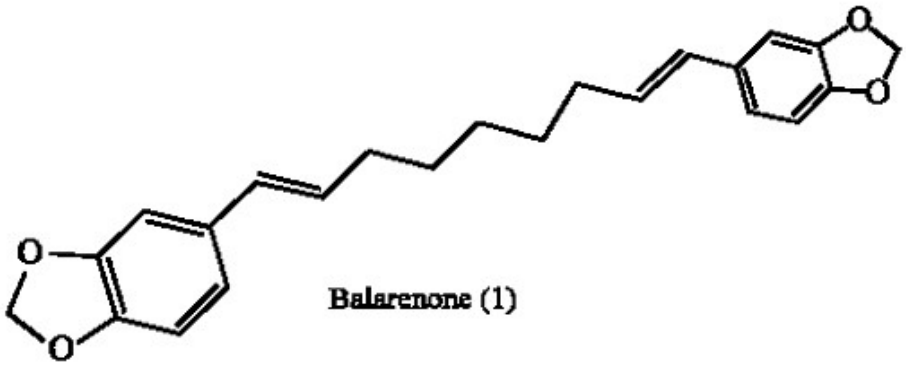
Vanillic acid (18)



Syringic acid (17)



6-hydroxyflavone (20)



Balarenone (1)

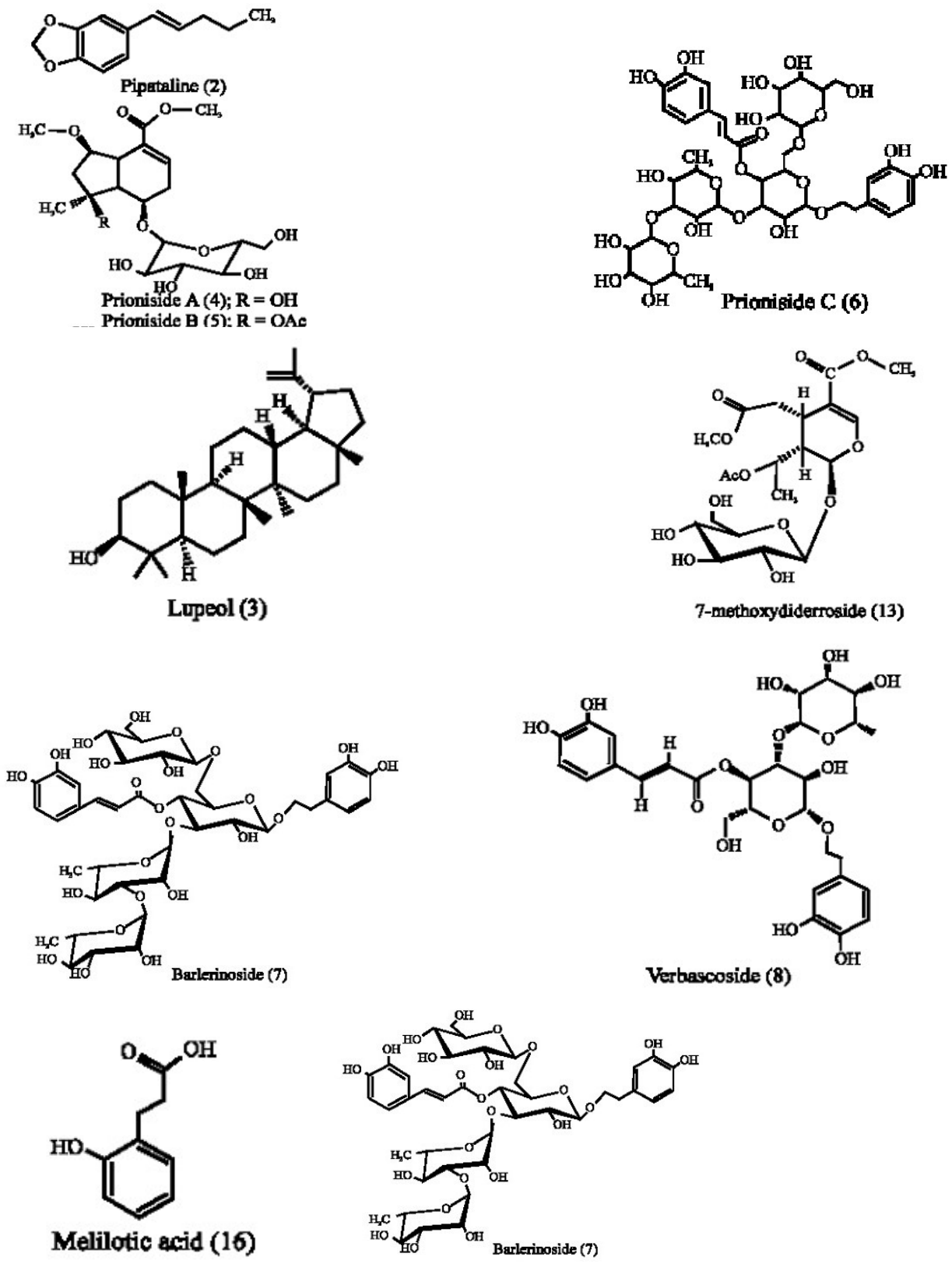


Fig. 5. Structures of some selected phytochemical isolated from B. prionitis Linn.

1.15. Pharmacological Activity

Antibacterial activity: It has been reported that different solvent (ether, ethanol and chloroform) extracts of B. prionitis leaves and callus showed antibacterial activity against numbers of gram positive bacterial isolates while no or slight inhibitions were observed against the aqueous extracts. Among these extracts, the ether extract showed strongest antibacterial activity. Some antibacterial phytochemicals include balarenone, pipataline and 13, 14-seco-stigmasta-5, 14-diene-3-a-ol have been isolated from the ethanolic extract of B. prionitis and these compounds showed strong antibacterial activity against Bacillus cereus and Pseudomonas aeruginosa. It was reported that the different solvent extracts of barks, leaves and stems showed potent antibacterial activity against oral pathogens Streptococcus mutans, Staphylococcus aureus, Pseudomonas aeruginosa and Bacillus cereus causing dental caries. Among the extracts, the methanolic bark extract showed more potent inhibitory activity against all the oral pathogenic bacteria. The antimicrobial activity of B. prionitis may be due to the presence of acetylbarlerin, barlerin, shanzhiside methyl ester, verbascoside, balarenone, pipataline, 13, 14-seco-stigmasta-5, 14-diene-3-a-ol and 6-O-acetyl shanzhiside methyl ester [34, 42].

Antifungal activity: The acetone, methanol and ethanol extracts of B. prionitis bark showed antifungal activity against oral pathogenic fungus Saccharomyces cerevisiae and two strains of Candida albicans. Among the extracts, methanolic extract was more potent against all the fungal isolates [51] reported that the petroleum ether, dichloromethane and ethanol extract of stem and root showed fungistatic and fungicidal activities against C. albicans.

Antiviral activity: Isolated two iridoid glycosides viz. 6-O-trans-p-coumaroyl-8-O-acetylshanzhiside methyl ester and its cis isomer from B. prionitis. In vitro study showed that these two glycosides posses potent antiviral activity against Respiratory Syncytial Virus (RSV) with EC50 and IC50 values of 2.46 and 42.2 μg mL-1, respectively [52].

Anthelmintic activity: The whole plant extract of B. prionitis was reported have anthelmintic activity [53]. In vitro study showed that aqueous and ethanolic extracts were significantly paralyzed the Pheretima posthuma worms at lower doses (50, 75 and 100 mg mL-1) and caused death over 100 mg mL-1 dose concentration in compare to standard drug albendazole [54].

Antifertility activity: The antifertility activity of B. prionitis roots was reported byoral administration of methanolic root extract (100 mg/rat/day) reduced the spermatogenesis in male albino rats. It was observed that the root extract decreased the production of round spermatids, sperm motility, spermatogonia, preleptotene spermatocytes population and mature leydig cells. Biochemical investigation revealed that the root extract was also reduced the total protein, glycogen, sialic acid contents of the testes, testicular glycogen contents, epididymides, ventral prostate and seminal vesicle. The antifertility effect of root extract may be due to the presence of iridoid glycosides barlerin and acetyl barlerin via affecting the functions of testicular somatic cells [55].

Antioxidant activity: The whole plant extract of B. prionitis was reported to show potent antioxidant activity. In vitro study showed that the ethanol and aqueous extracts of whole plant posses significant antioxidant activity against 1, 1-diphenyl-2-picrylhydrazyl (DPPH), 2, 2'-

azino-bis (3-ethylbenzothiazoline-6-sulphonic acid (ABTS), nitric oxide and hydroxyl radical scavenging assay and Fe3+ reduction assay. In compare to antioxidant potency, the ethanol extract was more potent than aqueous extract and its antioxidant potency showed sharp co-relation with the phenolic content of the extract [56] reported that the methanolic extract of roots, leaves and stems showed significant antioxidant property. It was observed that the leaves showed higher degree antioxidant potential and high phenolic content in comparison to flower and stem [57]. Some glycosides have been isolated from the aerial parts of B. prionitis namely barlerinoside, shanzhiside methyl ester, 6-O-trans-p-coumaroyl-8-O-acetylshanzhiside methyl ester, barlerin, acetylbarlerin, 7-methoxydiderroside and lupulinoside showed antioxidant activity. Among the isolated glycosides, only barlerinoside showed higher potential of antioxidant property with an IC50 value of 0.41 mg mL-1.

Anti-diarrheal activity: Reported the anti-diarrheal potential of butanol fraction of B. prionitis leaves. In vivo study showed that the butanol fraction dose dependently inhibited the castor oil induced diarrhea and PGE2 induced enteropooling in sprague-dawley rats. The butanol fraction also reduced the gastrointestinal motility in response to charcoal-induced gut transit changes [58].

Antidiabetic activity: Revealed that the alcoholic extract of B. prionitis leaves showed antidiabetic activity. Oral administration of alcoholic extract at dose concentration 200 mg kg-1 body weight significantly decreased the blood glucose, glycosylated hemoglobin level and increased serum insulin and liver glycogen level in diabetic rats. The extract also arrested the diabetes mediated weight loss [59]

Enzyme inhibitory effects: The extracts from the different parts and isolated phytochemicals of B. prionitis reported to inhibit the clinically significant enzymes, Acetylcholinesterase (AChE) and glutathione S-transferase (GST). Kosmulalage et al. (2007),Amoo et al. (2009, 2011) reported that the methanolic extracts of leaf, stem and root exhibited AChE inhibitory activities and the leaf and stem extracts exhibited higher potency of inhibition in compare the root extract. Several glycosides include barlerinoside, shanzhiside methyl ester, 6-O-trans-p-coumaroyl-8-O-acetylshanzhiside methyl ester, barlerin, acetylbarlerin, pataline, lupeol, 7-methoxydiderroside, 13, 14-seco-stigmasta-5, 14-diene-3-a-ol and lupulinoside have been isolated from the aerial parts of B. prionitis and these compounds showed different levels of AChE inhibitory activity. All these compounds and prioniside B and prioniside C also showed GST inhibitory activity of which prioniside B and prioniside C were more potential GST inhibitors [60].

Anti-inflammatory activity: Several reports demonstrated the usage of B. prionitis in the treatment of inflammations. The anti-inflammatory activity of B. prionitis was evaluated through in vitro enzyme based cyclooxygenase (COX-1 and COX-2) assays. It was found that the dichloromethane, petroleum ether and ethanol extracts of leaves, stems and roots exhibited significant inhibition of COX-1 and COX-2 with subsequent inhibition of prostaglandin synthesis that are involved in pain sensation. The Aqueous Fraction (TAF) of hydromethanolic extract of B. prionitis whole plant reported to have significant anti-inflammatory activity against the acute inflammation induced by carrageenan, histamine and dextran in rats [61]. The anti-

inflammatory activity of the 'TAF' may be due to the presence of iridoid glucosides, shanzhiside methyl ester, acetyl barlerin and barlein. Another study revealed that the aqueous extract fractions (FR-III and FR-IV) of root significantly inhibited the caragennan induced rat paw edema. The FR-III and FR-IV at oral dose concentration of 400 mg kg-1 body weight inhibited the paw edema by 50.64 and 55.76%, respectively and the results were comparable with the reference standard drug indomethacin with a 60.25% of inhibition. The ethanolic extract of flowers also exhibited anti-inflammatory activity in rats. Oral administration of flower extract (200 mg kg-1 body weight) showed significant dose-dependent reduction in carrageenin induced swelling and cotton pellet granuloma weight that were equivalent to 48.6 and 36.4% protectionn [62].

Cytoprotective activity: Mast cells play an important role in inflammatory responses and release histamine upon their degranulation to produce various allergic reactions.The hydro-methanolic extract of whole plant showed dose-dependent mast cells and erythrocyte membrane protection activity in response to the toxic chemicals. The extract inhibited the Compound 48/80 induced mast cells degranulation up to 64.91% at dose concentration 10 µg mL-1 and the result was comparable with the reference standard disodium cromoglycate (10 µg mL-1) with 19.32% protection (Maji et al., 2011). The extract (10 µg mL-1) provided significant erythrocyte membrane protection (27.10%) against hypotonicity haemolysis and the result was comparable with reference standard indomethacin (10 µg mL-1) with 61.29% protection [63].

Diuretic effect: The diuretic property of B. prionitis flower extract was performed by the oral administration of aqueous flower extract (200 mg kg-1) was significantly increased the urination (dieresis) and sodium elimination but not potassium in rats. The diuretic effect of flower extract (200 mg kg-1) was comparable and statistically significant with the reference drug furosemide (20 mg kg-1) [64].

Anti-nociceptive activity: The analgesic activity of B. prionitis flowers was evaluated using an Ugo Basile Analgesy meter induced artificial pain and acetic acid induced writhing models. In vivo study showed that the flower extract dose dependently provided a significant increase in the analgesio-meter-induced force and exhibited significant resistance against pain in mice. The flower extract was also provided dose dependent significant reduction in writhing characterizes by the reduction in acetic acid induced abdominal cramping and abdominal cramping. At a dose concentration of 50 mg kg-1 body weight, the extract provided statistically significant reduction of writhing by 5.24% [65].

Hepatoprotective activity: The iridoid glycosides enriched fraction from hyrdoethanolic extract of leaves and stems of B. prionitis was reported to show significant hepatoprotection against carbon tetrachloride, galactosamine and paracetamol induced hepatotoxicity in mice and rats (Singh et al., 2005). The oral administration of iridoid fraction significantly reduced the hepatotoxin induced elevated levels of serum alanine aminotransferase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), bilirubin and triglycerides in a dose dependent manner. The fraction was also increased the hepatic glutathione content and reduced the hepatic lipid peroxidation in response to the hepatotoxicity in mice and rats [66].

Anti-arthritic activity: The TAF fraction was reported to have anti-arthritic property in Mycobacterium tuberculosis induced adjuvant arthritis rats model. The TAF at oral dose range of 12.5-100 mg kg-1 significantly inhibited leucocytes migration and lowered the Erythrocyte Sedimentation Rate (ESR) and exudate volume in pleural cavity which indicated the inhibition of vascular permeability in arthritis-induced rats protection [67].

Antihypertensive activity: In a study, antihypertensive In a study, antihypertensive activity was evaluated in male albino Wistar rats, which were uninephrectomized. Hypertension was induced by injecting deoxycorticosterone acetate salt, rats were divided into five groups, different dose levels were administered twice a week for the duration of 6 weeks, and instead of water, 1% NaCl was provided for drinking to the rats. Dose levels of 200 mg/BW and 400 mg/BW showed the maximum antihypertensive effect among all. Significant antihypertensive activity is developed by the alkaloids, flavonoids, steroids, saponins, tannin, and phenolic compounds, whose presensce in B. prionitis was confirmed through phytochemical screenings [68].

Central nervous system (CNS) activity:CNS activity of the 70% ethanol extract of leaves of B. prionitis Linn (Acanthaceae) in Swiss albino mice was estimated. General behavior was studied using actophotometer. According to the study, it was observed that the test drug has the stimulant activity. However, in comparison with the standard drug, namely, fluoxetine hydrochloride available in the market, the stimulant activity seemed to be less. Fluoxetine stimulates activity in the animals was found to be 91.93%, whereas the test drug from B. prionitis stimulated the animal only by 49.72%. The results suggested that ethanol extract of B. prionitis exhibits antidepressant activity in testing animal models [69].

Glutathione S-transferase, acetylcholinesterase inhibitory activity: A new compound, balarenone, along with three known compounds, pipataline, lupeol, and 13,14-seco-stigmasta-5,14-diene-3-α-ol was isolated from the ethanolic extract of B. prionitis of Sri Lankan origin. All four of these expressed moderate inhibitory activity against the enzymes glutathione S-transferase and acetylcholinesterase [70].

1.16 Toxicity

The toxicity study with the alcoholic extract of roots and leaves of B. prionitis did not showed any toxic effects in adult albino rats (Dheer and Bhatnagar (2010). No death was observed up to the oral administration of extract dose concentration 2.5 g kg-1 body weight during the 14 days of study period Dheer and Bhatnagar (2010). Singh et al. (2005) reported that the iridoid glucosides rich aqueous fraction B. prionitis did not produced any signs of abnormalities or any mortality up to the single oral administration of 3000 mg kg-1 dose in mice during the 15 days of study period. However, the intraperitoneal LD50 was determined as 2530 mg kg-1 for the aqueous fraction in mice (Singh et al., 2005).

1.17. Phytoconstituents in B. prionitis

Secondary metabolites play an essential role for the economic importance of medicinal plants, although it's not only economical also a core prospective for the betterment of our health. Preliminary phytochemical screening showed presence of phytochemicals such as alkaloid (by Mayer's reagent test, Hager's reagent test, Wagner's reagent test, and Dragendorff 's reagent

test), flavonoids (by alkaline reagent test and Shinoda test), saponins (Frothing test), terpenoids (dinitrophenylhydrazine test), phytosterol (Liebermann's test and Liebermann–Burchard test), phenolic compound and tannin ($FeCl_3$, lead acetate test, and bromine water test), essential oil, proteins, and amino acids (Millon's test, Biuret test, and ninhydrin test), carbohydrates (Molisch test, Fehling's solution A, Fehling's solution B, and Benedict's test), glycosides (Borntrager's test and legal's test) [71-72]. Its aerial parts contain glycosides such as barlerinoside, shanzhiside methyl ester, lupulinoside, 7-methoxydiderroside barlerin, acetylbarlerin, and verbascoside 73-74]; terpenoid such as lupeol, pipataline, and balarenone; and flavones such as apigenin 7-O-β-D-glucoside [75] and luteolin-7-o-glucoside [74]. Leaves were reported to contain phenolic acids such as Melilotic acid [76], syringic acid, vanillic acid, and p-hydroxybenzoic acid and flavones such as 6-hydroxyflavone and scutellarin [77]. Roots contain phytosterol BS [78].

2. CONCLUSION

This study has confirmed antimicrobial potential of the plant B. prionitis, thus supporting its folklore application as preventive remedy against oral microbial diseases. The efficacy of *Barleria prionitis* extract mouthwash in comparison with gold standard chlorhexidine (CHX) mouthwash on the oral health was reported. Within the limitation of this trial, herbal mouthwash has been shown to demonstrate similar effects on plaque as compared to the standard drug CHX. Further long term research needs to be done to check the efficacy and effectiveness of herbal products over standard drug regime.

There is a very high prevalence of Periodontal diseases and caries in India, according to many studies.[79] Majority of population gives a low precedence to oral health which may be attributed to such high prevalence of oral diseases. Other reasons for such high prevalence may be lack of availability of simple interventions to rural and underprivileged people and lack of basic oral health education.[80]

Antimicrobial agents may aid in disrupting pathogenic bacteria associated with plaque, thus aiding in the control of gingivitis.[81] Healthy oral flora is influenced by effective plaque control; however, the pathogenic degree of the bacteria in plaque also plays a significant role, as does the host response, immune status, and amount of time that plaque remains on the tooth. The World Health Organization estimates that 65–80% of the world's population uses traditional medicine as the primary form of health care. This study was an attempt to investigate if indigenously prepared mouthwashes from *B. prionitis* can effectively reduce plaque and gingival scores in the selected population.

This study focused on two specific mouth rinses: *B. prionitis* rinse and 0.12% CHX rinse (CHX), both claiming to be effective in the treatment of dental plaque. CHX (0.12%) has the American Dental Association (ADA) Seal of Acceptance and is Food and Drug Administration approved for the reduction of plaque and gingivitis. CHX also has long-standing research to substantiate its safety 13–16 and efficacy, whereas the herbal rinse mouth rinse used in this study is a newer, less researched product [82-83].

A variety of chemotherapeutic agents have been examined for their ability to control oral micro-organisms and to affect plaque formation. CHX digluconate has a 30 years history in Dental Medicine. Studies showed that the most disturbing side-effect of Chlorhexidine is extrinsic tooth staining and others such as unpleasant taste and burning sensation. There is rising awareness in the result of natural compounds as they have dual effect. On one hand they inhibit the growth of bacterial organisms which are associated with oral diseases and on other hand they uphold the growth of helpful microorganisms.[84]

B. prionitis mouth washes was prepared based on the findings of an *in vitro* study conducted by Aneja *et al*. and Diwan. In this study, 50% extracts of *B. prionitis* was found to be most effective in inhibiting *Streptococcus mutans*.

To make the taste agreeable some amount of artificial sweetening agents were added. Flavoring agents like menthol, thymol, etc., are essential oils. Essential oils are excellent plaque inhibitors as chlorhexidine so they may act as confounders in plaque and gingival evaluation that's why they are not added in preparation.[85]

A study by Aneja *et al*.[87] and Diwan and Gadhikar[88] have showed the antibacterial action of *B. prionitis in vitro* but there are no published reports on the antibacterial action of *B. prionitis in vivo*. So, this research can be considered as the only research in this aspect which limits its comparison with other such studies.

The antimicrobial potency of plants is believed to be due to tannins, saponins, phenolic compounds, essential oils and flavonoids (Cowan, 1999). The antimicrobial potency of *B. prionitis* may be due to the presence of five iridoid glucoside esters, acetyl barlerin (6, 8-di-O-acetyl shanzhiside methyl ester), barlerin (8-O-acetyl shanzhiside methyl ester), shanzhiside methyl ester and 6-0-acetyl shanzhiside methyl ester, verbascoside (6-*O*-trans-p-coumaroyl-8-O-acetylshanzhiside methyl ester)[86, 88, 89].

It is interesting to note that even crude extracts of *B. prionitis* showed good activity against dental caries causing oral pathogens where modern antibiotic therapy has failed [86].

In the present study, Barleria prionitis has shown a good potential as an anti-plaque agent. Barleria prionitis has been proven to be less effective than CHX. Subjects answered the questionnaire that they found Barleria prionitis to be effective and convenient to use due taste duration (aftertaste) in their mouth after rinsing, taste was better than CHX due to the of natural ingredients.

In regard to the efficacy of plaque reduction, CHX was considered to be more effective. However, CHX rinsing can cause a number of local side effects[90, 91, 92] including extrinsic tooth and tongue brown staining, taste disturbance, enhanced supragingival calculus formation and less commonly, desquamation of the oral mucosa. Due to the side-effects of CHX users are not bale to accept CHX completely and for long-term use [93]. Barleria prionitis doesn’t have any side-effects due to its natural ingredients. It can be use as a good replacement to patients who wish to avoid alcohol, sugar, any artificial preservatives and artificial colors in their mouthrinses. Further studies of longer time period have to be conducted. The natural product in issue has to be compared to both positive as well as negative control [94-110]. B. prionitis occupy a significant

place in the Ayurvedic medicine in India. The detailed information as provided in this review on its traditional uses, phytochemistry, pharmacology and toxicity of the extracts of different parts might be added value in the scientific evaluation of medicinal use of this plant. Extensive literature survey revealed the promising pharmacological includes antimicrobial, anthelmintic, antifertility, antioxidant, antidiabetic, anti-inflammatory, anti-arthritic, cytoprotective, hepatoprotective, anti-diarrhoeal, enzyme inhibitory, diuretic and anti-nociceptive activities of the extract and isolated molecules of this plant without any toxic effects. In future study, the conversion of these pharmacological activities in to the modern drugs, proper scientific evaluation includes isolation of responsible phytochemicals, their mechanism of actions, toxicity and proper standardization need to be explored.

3. ACKNOWLEDGEMENT

The authors are grateful to Management and also thankful to Dr. V. M. Shastry, Principal of Gangamai College of pharmacy, Nagaon Dhule, India and Smt. S. S. Patil College of Pharmacy, Chopda, India for his assistance for carrying out this work.

4. REFERENCES

1. Poul Erik Petersen. (2003). The World Oral Health Report, Oral Health Programme Noncommunicable Disease Prevention and Health Promotion World Health Organization Geneva, Switzerland, 1-14.

2. Cirino S.M., Scantlebury S. (1998). Dental caries in developing countries. Preventive and restorative approaches to treatment, The New York state dental journal 64(2), 32-9.

3. Loesche, W.J. (1986). Role of Streptococcus mutans in human dental decay. Microbiological Reviews, 50, 353- 380.

4. Gibbons, Robert., "What is Economic Sociology and Should any Economists Care?" *Journal of Economic Perspectives*, 19 (1), 3-7 (2005).

5. Tanzer, J. M., J. Livingston. (2001). The Microbiology of Primary Dental Caries in Humans. *Journal of Dental Education*, 65(10), 1028-1037.

6. Marsh, P.D. (1994). Microbial Ecology of Dental Plaque and Its Significance in Health and Disease. *Advances in Dental Research*, 8, 263-271.

7. Keyes, P.H. (1960). The Infectious and Transmissible Nature of Experimental Dental Caries. *Archives of Oral Biology*, 1, 304-320.

8. Montenegro R, Needleman I, Moles D, Tonetti M. (2002). Quality of RCTs in periodontology--a systematic review. *Journal of Dental Research*, 81(12), 866-870.

9. Faggion CM, Jr., Atieh MA, Park S. (2013). Search strategies in systematic reviews in periodontology and implant dentistry. *Journal of Clinical Periodontology*, 40(9), 883-888.

10. Faggion CM, Jr., Giannakopoulos NN. (2013). Critical appraisal of systematic reviews on the effect of a history of periodontitis on dental implant loss. *Journal of Clinical Periodontology*, 40(5), 542-552.

11. Glenny AM, Esposito M, Coulthard P, Worthington HV. (2003). The assessment of systematic reviews in dentistry. *European Journal of Oral Sciences*, 111(2), 85-92.

12. Clarkson JE, Ramsay CR, Eccles MP. (2010). The translation research in a dental setting (TRiaDS) programme protocol. *Implementation Science*, 5:57.

13. Shea BJ, Bouter LM, Peterson J, Boers M, Andersson N, Ortiz Zea. (2007). External validation of a measurement tool to assess systematic reviews (AMSTAR). PLOS ONE, 2 (12), e1350.

14. Dey, S.K., D. Banerjee, P.K. Nandi, S. (2009). Chattopadhyay and K. B. Karmakar, Antimicrobial properties of Indian spices. *Natural Prod.,* 5: 104-110.

15. Ansari, J.A. and N.N. (2010). Inamdar, The promise of traditional medicines. *Int. J. Pharmacol.,* 6, 808-812.

16. Shafaei, A., E. Farsi, B.M.K. Ahamed, M.J.A. Siddiqui, I.H. Attitalla, I. Zhari and M.Z. Asmawi, (2011). Evaluation of toxicological and standardization parameters and phytochemical investigation of Ficus deltoidea leaves. *Am. J. Biochem. Mol. Biol*., 1, 237-243.

17. Ramachandran, S., M. Vamsikrishna, K.V. (2011). Gowthami, B. Heera and M.D. Dhanaraju, Assessment of cytotoxic activity of agave cantula using brine shrimp (Artemia salina) lethality bioassay. *Asian J. Sci. Res.,* 4, 90-94.

18. Menghani, E., A. Pareek, R.S. Negi and C.K. Ojha. (2011).Search for antimicrobial potentials from certain indian medicinal plants. *Res. J. Med. Plant,* 5, 295-30.

19. Kumar, T. and K.S. Chandrashekar, Bauhinia purpurea Linn.: (2011). A review of its ethnobotany, phytochemical and pharmacological profile. *Res. J. Med. Plant*, 5, 420-431.

20. Musyimi, D.M., J.A. Ogur and P.M. Muema (2008). Phytochemical compounds and antimicrobial activity of extracts of aspilia plant (Aspilia mossambicensis) (Oliv) wild. *Int. J. Bot.*, 4, 56-61.

21. Mohajer, M., P. Sarkhail, N. Hajarolasvadi, M.J. Zamani and R. Khorasan. (2006). Antiinflammatory and analgesic effects of Phlomis lanceolata boiss. and hohen. extracts and examination of their components. *Int. J. Pharmacol*., 2, 50-54.

22. Dey, S.K., D. Banerjee, S. Chattapadhyay and K.B. Karmakar. (2010). Antimicrobial activities of some medicinal plants of West Bengal. *Int. J. Pharma Bio. Sci*., 1, 1-10.

23. Roy, S. and D. Banerjee, (2010). Isolation of antimicrobial compound by endophytic bacteria from Vinca rosea. *Int. J. Curr. Res*., 5, 47-51.

24. Kayode, A.A.A. and O.T. Kayode, (2011). Some medicinal values of Telfairia occidentalis: A review. *Am. J. Biochem. Mol. Biol*., 1, 30-38.

25. Saadabi, A.M.A., A.G. AL-Sehemi and K.A. AL-Zailaie, (2006). In vitro antimicrobial activity of some Saudi Arabian plants used in folkloric medicine. *Int. J. Bot*., 2, 201-204 .

26. Mukherjee, P.K., D. Mukherjee, A.K. Maji, S. Rai and M. Heinrich. (2009). The sacred lotus (Nelumbo nucifera)-phytochemical and therapeutic profile. *J. Pharm. Pharmacol.,* 61, 407-422.

27. Sohail, M.N., F. Rasul, A. Karim, U. Kanwal and I.H. Attitalla (2011). Plant as a source of natural antiviral agents. *Asian J. Anim. Vet. Adv*., 6, 1125-1152.

28. Gantait, A., A. Maji, T. Barman, P. Banerji, P. Venkatesh and P.K. Mukherjee. (2011). Estimation of capsaicin through scanning densitometry and evaluation of different varieties of capsicum in India. *Nat. Prod. Res.,* 26, 216-222.

29. Agrawal, B., S. Das and A. Pandey, Boerhaavia diffusa Linn: (2011). A review on its phytochemical and pharmacological profile. *Asian J. Applied Sci.,* 4, 663-684.

30. Bele, A.A., V.M. Jadhav and V.J. Kadam, Potential of tannins: (2010). A review. *Asian J. Plant Sci*., 9, 209-214.

31. Khare, C.P., Indian Herbal Remedies: (2004). Rational Western Therapy, Ayurvedic and Other Traditional Usage, Botany. 1st Edn., Springer, New York, pp: 93-94.

32. Khare, C.P. (2007). Indian Medicinal Plants: An Illustrated Dictionary. 1st Edn., Springer Science, New York, pp: 82-83.

33. Daniel, M. (2006). Medicinal Plants: Chemistry and Properties. 1st Edn., Science Publishers, USA., Pages: 78.

34. Aneja, K.R., R. Joshi and C. Sharma. (2010). Potency of Barleria prionitis L. bark extracts against oral diseases causing strains of bacteria and fungi of clinical origin. *New York Sci. J.,* 3, 5-12.

35. Shendage, S.M. and S.R. Yadav. (2010). Revision of the Genus Barleria (Acanthaceae) in India. Rheedea, 20, 81-130.

36. Singh, M.P. and H. Panda, (2006). Medicinal Herbs With their Formulations. Vol. 1, Daya Publishing House, New Delhi, pp: 155-156.

37. Kamble, M.Y., S.R. Pal, S.M. Shendage, G.B. Dixit, P.D. Chavan, U.S. Yadav and S.R. Yadav, (2007). Promising Indian Barlerias of Ornamental Potential. In: Underutilized and Underexploited Horticultural Crops, Peter, KV. (Ed.). Vol. 1. New India Publishing Agency, New Delhi, pp: 144.

38. Dassanayake, M.D. (1998). A Revised Handbook to the Flora of Ceylon. Vol. 12, CRC Press, Boca Raton, USA., Pages: 87.

39. Shukla, P., A. Singh, S. Gawri, A. Alexande and S. Sonwane (2011). In vitro propagation of Barleria prionitis Linn and its antibacterial activity. *Int. J. Pharma Prof. Res.,* 2: 198-200.

40. Khadse, C.D. and R.B. Kakde (2011). Anti-inflammatory activity of aqueous extract fractions of Barleria prionitis L. roots. Asian J. Plant Sci. Res., 1, 63-68.

41. Maji, A.K., S. Bhadra, S. Mahapatra, P. Banerji and D. Banerjee, (2011). Mast cell stabilization and membrane protection activity of Barleria prionitis L. *Pharmacog. J.,* 3, 67-71.

42. Kosmulalage, K.S., S. Zahid, C.C. Udenigwe, S. Akhtar, A. Ata and R. Samarasekera, (2007). Glutathione S-transferase, acetylcholinesterase inhibitory and antibacterial activities of chemical constituents of Barleria prionitis. Z. Naturforsch., 62b, 580-586.

43. Taneja, S.C. and H.P. Tiwari, Structures of two new iridoids from Barlrria prionitis Linn. Tetrahedron Lett., 16, 1995-1998 (1975).

44. Singh, B., B.K. Chandan, A. Prabhakar, S.C. Taneja, J. Singh and G.N. Qazi. (2005). Chemistry and hepatoprotective activity of an active fraction from Barleria prionitis Linn. in experimental animals. Phytother. Res., 19, 391-404.

45. Chen, J.L., P. Blanc, C.A. Stoddart, M. Bogan and E.J. Rozhon. (1998). New iridoids from the medicinal plant Barleria prionitis with potent activity against respiratory syncytial virus. *J. Nat. Prod.,* 61, 1295-1297.

46. Ata, A., K.S. Kalhari and R. Samarasekera. (2009). Chemical constituents of Barleria prionitis and their enzyme inhibitory and free radical scavenging activities. *Phytochem. Lett.,* 2, 37-40.

47. Ganga Raju, S.V., K.C. Naidu, V. Chakradhar and R.Y. Prasad. (2002). Anthraquinones from Barleria prionitis. *Indian Drugs*, 39, 400-401.

48. Gupta, H.M. and V.K. Saxena. (1984). A new acylated luteolin-7-O-β-D-glucoside from the roots of Barleria prionitis (Linn.). *Natl. Acad. Sci. Lett*., 7, 187-189.

49. Harborne, J.B., S.S. Subramanian and A.G.R. Nair, (1971). Scutellarein 7-rhamnosyglucoside from Barleria prionitis. *Phytochemistry,* 10, 2822-2823.

50. Gupta, R.S., P. Kumar, V.P. Dixit and M.P. Dobhal. (2000). Antifertility studies of the root extract of the Barleria prionitis Linn in male albino rats with special reference to testicular cell population dynamics. *J. Ethnopharmacol*., 70, 111-117.

51. Amoo, S.O., A.R. Ndhlala, J.F. Finnie and J. Van Staden. (2011). Antifungal, acetylcholinesterase inhibition, antioxidant and phytochemical properties of three Barleria species. S. *Afr. J. Bot*., 77, 435-445.

52. Chetan, C., M. Suraj, C. Maheshwari, A. Rahul and P. Priyanka. (2011). Screening of antioxidant activity and phenolic content of whole plant of barleria prionitis linn. *Int. J. Res. Ayurveda Pharm.*, 2, 1313-1319.

53. Chavan, C.B., M.G. Hogade, S.D. Bhinge, M. Kumbhar and A. Tamboli. (2010). In vitro anthelmintic activity of fruit extract of Barleria prionitis Linn. against Pheretima posthuma. *Int. J. Pharm. Pharm. Sci.,* 2, 49-50.

54. Chavan, C.B., U.V. Shinde, M. Hogade, and S. Bhinge. (2010). Screening of In-vitro antibacterial assay of Barleria prionitis Linn. *J. Herb. Med. Toxicol*., 4, 197-200.

55. Verma, P.K., A. Sharma, S.C. Joshi, R.S. Gupta and V.P. Dixit, (2005). Effect of isolated fractions of Barleria prionitis root methanolic extract on reproductive function of male rats: Preliminary study. *Fitoterapia,* 76, 428-432.

56. Amoo, S.O., J.F. Finnie and J. van Staden. (2009). In vitro pharmacological evaluation of three Barleria species. *J. Ethanopharmacol*., 121, 274-277.

57. Jaiswal, S.K., M.K. Dubey, A.K. Verma, S. Das, M. Vijaykumar and C.V. Rao. (2010). Evaluation of iridoid glycosides from leave of Barleria prionitis as an anti-diarrhoeal activity: An Ethnopharmacological study. *Int. J. Pharm. Sci*., 2, 680-686.

58. Jaiswal, S.K., M.K. Dubey, S. Das, A.R. Verma and C.V. Rao, (2010). A comparative study on total phenolic content, reducing power and free radical scavenging activity of aerial parts of Barleria prionitis. *Int. J. Phytomed*., 2, 155-159.

59. Dheer, R. and P. Bhatnagar. (2010). A study of the antidiabetic activity of Barleria prionitis Linn. *Ind. J. Pharm*., 42, 70-73.

60. Ata, A., S.A. van den Bosch, D.J. Harwanik and G.E. Pidwinski, (2007). Glutathione S-transferase and acetylcholinesterase-inhibiting natural products from medicinally important plants. *Pure Appl. Chem*., 79, 2269-2276.

61. Singh, B., S. Bani, D.K. Gupta, B.K. Chandan and A. Kaul. (2003). Anti-inflammatory activity of TAF an active fraction from the plant Barleria prionitis Linn. *J. Ethanopharmacol*., 85, 187-193.

62. Jaiswal, S.K., M.K. Dubey, S. Das, A.R. Verma, M. Vijayakumar and C.V. Rao. (2010). Evaluation of flower of Barleria prionitis for anti-inflammatory and anti-nociceptive activity. *Int. J. Pharm. Biol. Sci.,* 1, 1-10.

63. Manek, R.A., N.R. Sheth, J.D. Vaghasiya, S.V. Malaviya, N.P. Jivani and J.R. Chavda, (2011). Study on herb-herb interaction potential of Glycyrrhiza glabra with Solanum xanthocarpum and Adhatoda vasica on mast cell stabilizing activity. *Int. J. Pharmacol*., 7, 589-598.

64. Musale, S.B., V.A. Jagtap, M.S. Patil, K.P. Chittam and K.P. Wagh. (2011). Diuretic activity of Barleria prionitis Linn Flower extract. *Int. J. Drug Discovery Herbal Res*., 1, 20-21.

65. Sawarkar HA, Kashyap PP, Pandey AK, Singh MK, Kaur CD. (2016). Antimicrobial and cytotoxic activities of Barleria prionitis and Barleria grandiflora: A comparative study. *Bangladesh J Pharmacol*,11, 802-9.

66. Gangopadhyay A, Malakar J, Ghosh A, Deb J, Dey S, Datta S. (2012). The central nervous system activity of Barleria prionitis Linn, on the locomotor activity of Swiss albino mice using actophotometer. *Int J Pharm Biol Sci Arch*, 3(2), 403-5.

67. Jeyasankar A, Premalatha S, Krishnappa K, Elumalai K. (2013). Larvicidal activity of Barleria prionitis L (Acanthaceae) against Japanese encephalitis vector, Culex tritaeniorhynchus giles (Diptera: Culicidae). *Int J Inf Res Rev*, 1(2),116-20.

68. Sawarkar HA, Kashyap PP, Pandey AK, Singh MK, Kaur CD. (2016). Antimicrobial and cytotoxic activities of Barleria prionitis and Barleria grandiflora: A comparative study. *Bangladesh J Pharmacol*,11, 802-9.

69. Choudhary M, Kumar V, Gupta PK, Singh S. (2014). Anti-arthritic activity of Barleria prionitis Linn, leaves in acute and chronic models in Sprague Dawley rats. Bull Fac Pharm Cairo Univ, 52(2), 199-209.

70. Kalhari KS, Zahida S, Udenigwea CC, Akhtara S, Ata A, Samarasekera R. (2007). Glutathione S-transferase, acetylcholinesterase inhibitory and antibacterial activities of chemical constituents of Barleria prionitis. Z Naturforsch, 62(b), 580-6.

71. Kalhari KS, Zahida S, Udenigwea CC, Akhtara S, Ata A, Samarasekera R. (2007). Glutathione S-transferase, acetylcholinesterase inhibitory and antibacterial activities of chemical constituents of Barleria prionitis. Z Naturforsch, 62(b), 580-6.

72. Chetan C, Suraj M, Maheshwari C, Rahul A, Priyanka P. (2011). Screening of antioxidant activity and phenolic content of whole plant of Barleria prionitis Linn. *Int J Res Ayurveda Pharm*, 2(4), 1313.

73. Chen JL, Blanc P, Stoddart CA, Bogan M, Rozhon EJ, Parkinson N. (1998). New iridoids from the medicinal plant Barleria prionitis with potent activity against respiratory syncytial virus. *J Nat Prod,* 61,1295-7.

74. Ata A, Kalhari KS, Samarasekera R. (2009). Chemical constituents of Barleria prionitis and their enzyme inhibitory and free radical scavenging activities. *Phytochem* Lett, 2 Suppl ,37-40.

75. Aneja KR, Joshi R, Sharma C. (2010). Potency of Barleria prionitis L, bark extracts against oral diseases causing strains of bacteria and fungi of clinical origin. N Y Sci J, 3, 5-12.

76. Daniel M, Sabnis SD. (1987). Chemosystematics of some Indian members of the Acanthaceae proc. *Indian Acad Sci Plant Sci*, 97:315.

77. Daniel M. (2006). Medicinal Plants: Chemistry and Properties. 1st ed. USA: Science Publishers; 2006.

78. Singh K, Gupta RS. (2016). Anti fertility activity of β-sisolated from Barleria prionitis (l), roots in male albino rats. *Int J Pharm Pharm Sci,* 8(5); 88-96.

79. Shaju JP, Zade RM, Das M. (2011). Prevalence of periodontitis in the Indian population: A literature review. *J Indian Soc Periodontol*., 15, 29–34.

80. Addy M, Griffiths G, Dummer P, Kingdom A, Shaw WC. (1987). The distribution of plaque and gingivitis and the influence of toothbrushing hand in a group of South Wales 11-12 year-old children. *J Clin Periodontol*., 14, 564–72.

81. Hannah JJ, Johnson JD, Kuftinec MM. (1989). Long-term clinical evaluation of toothpaste and oral rinse containing *Sanguinaria* extract in controlling plaque, gingival inflammation, and sulcular bleeding during orthodontic treatment. *Am J Orthod Dentofacial Orthop*., 96, 199–207.

82. Van Dyke TE, Offenbacher S, Pihlstrom B, Putt MS, Trummel C. (1999). What is gingivitis?. Current understanding of prevention, treatment, measurement, pathogenesis and relation to periodontitis. *J Int Acad Periodontol*., 1, 3–15.

83. Scherer W, Gultz J, Lee SS, Kaim J. (1998). The ability of an herbal mouthrinse to reduce gingival bleeding. *J Clin Dent*., 9, 97–100.

84. Percival RS, Devine DA, Duggal MS, Chartron S, Marsh PD. (2006). The effect of cocoa polyphenols on the growth, metabolism, and biofilm formation by *Streptococcus mutans* and *Streptococcus sanguinis*. *Eur J Oral Sci.,* 114, 343–8.

85. Claffey N. Essential oil mouthwashes: (2003). A key component in oral health management. *J Clin Periodontol*., 30(Suppl 5), 22–4.

86. Aneja KR, Joshi R, Sharma C. (2010). Potency of *Barleria prionitis* L. bark extracts against oral diseases causing strains of bacteria and fungi of clinical origin. *N Y Sci J*., 3, 5–12.

87. Diwan PD, Gadhikar YA. (2012). Assessment of phytochemical composition and antibacterial activity of different extracts of *Barleria prionitis* leaves against oral microflora to improve dental hygiene. *Asian J Pharm Clin Res*., 5, 182–4.

88. Suri JL, Banerjee SK, Taneja SC, Chandra S, Anand AS, Prabhakar A. (2003). United States Patent Application Publication, 20030181397.

89. Chen JL, Blanc P, Stoddart CA, Bogan M, Rozhon EJ, Parkinson N. (1998). New iridoids from the medicinal plant *Barleria prionitis* with potent activity against respiratory syncytial virus. *J Nat Prod*., 61,1295–7.

90. Gupta D, Jain A. (2015). Effect of Cinnamon Extract and Chlorhexidine Gluconate (0.2%) on the Clinical Level of Dental Plaque and Gingival Health: A 4-Week, Triple-Blind Randomized Controlled Trial. *J Int Acad Periodontol*., 17, 91–8.

91. Gupta D, Gupta RK. (2015). Investigation of antibacterial efficacy of Acacia nilotica against salivary mutans streptococci: A randomized control trial. Gen Dent., 63, 23–7.

92. Gupta D, Devaki M, Dommaraju N, Srinivas KT, Patil AA, Momin RK. (2015). CAM Modalities for Musculoskeletal Pain Management Among Dental Professionals of East India. Holistic nursing practice., 29, 385–90.

93. Gupta D, Momin RK, Mathur A, Srinivas KT, Jain A, Gupta RK. (2015). Prevalence of Dental Caries and Treatment Needs in 3-5-Year-Old Preschool Children in Rural Moradabad District, India. *North American journal of medical sciences*, 7, 143–50.

94. Gupta D, Mathur A, Patil GI, Tippanawar HK, Jain A. (2014). Prevalence of musculoskeletal disorder and alternative medicine therapies as a treatment modality for it among dentists of North India: A descriptive study. *Pharmacognosy Research,* 7, 350–4.

95. Gupta D, Nayan S, Tippanawar HK, Patil GI, Jain A, Gupta RK. (2015). Are herbal mouthwash efficacious over chlorhexidine on the dental plaque? *Pharmacognosy Research,* 7, 277–81.

96. Gupta D, Gupta RK, Bhaskar DJ, Gupta V. (2015). Comparative Evaluation of Terminalia chebula Extract Mouthwash and Chlorhexidine Mouthwash on plaque and gingival inflammation – 30 days randomized control trial. *Oral Health Preventive Dentistry*, 13, 5–12.

97. Gupta D, Somasundaram, Kumaran NS, Batra N, Sardiwal KK, Mahajan S. (2014). Acupuncture and Dentistry. *Oral Health and Dental Management*, 13,1–9.

98. Gupta D, Nagar P, Karim B, Khan IM, Naveen B, Chaturvedi M. (2014). Tobacco abuse amongst the school going students of 15 to 18 years of Almora district, Uttarakhand: A cross sectional study. *Oral Health and Dental Management*, 13, 680–6.

99. Devanand G, John BD, Rajendra GK, Bushra K, Alpana K, Ankita J. (2014). Use of complementary and alternative medicine for work related musculoskeletal disorders associated with job contentment in dental professionals: Indian outlook. *Ethiopian Journal of Health Sciences*, 24, 117–124.

100. Gupta D, Dalai DR. (2014). Acupuncture (zhēn jiǔ) - An emerging adjunct in routine oral care. *J Tradit Complement Medicine*, 4, 218–23.

101. Gupta D, Bhaskar DJ, Gupta RK, Jain A, Yadav P, Dalai DR. (2014). Is CAM therapy effective in job satisfaction among dentist of with Musculoskeletal Disorders: A cross sectional Study. Medycyna Pracy., 65, 317–23.

102. Gupta D, Bhaskar DJ, Gupta RK, Karim B, Jain A, Singh R. (2014). Efficacy of *Ocimum sanctum* extract mouthwash in comparison with Chlorhexidine Mouthwash on dental plaque and gingival inflammation – A Randomized Control Clinical Trial. *Journal of Ayurveda and Integrative Medicine,* 5,109–16.

103. Gupta D, Batra R, Mahajan S, Bhaskar DJ, Jain A, Shiju M. (2014). Comparative Evaluation of the Complementary and Alternative Medicine Therapy and Conventional Therapy Use for Musculoskeletal Disorders Management and Its Association with Job Satisfaction among Dentists of West India. *J Tradit Complement Med*., 4, 263–7.

104. Kumar GR, Devanand G, John BD, Ankit Y, Khursheed O, Sumit M. (2014). Preliminary antiplaque efficacy of *Aloe Vera* mouthwash on 4 day plaque re-growth model: Randomized control trial. *Ethiopian Journal of Health Sciences*, 24,139-144.

105. Gupta D, Bhaskar DJ, Gupta RK, Karim B, Gupta V, Punia H. (2014). Effect of Terminalia chebula Extract and Chlorhexidine on salivary pH and periodontal health: 2 Weeks Randomized Control Trial. *Phytotherapy Research*, 28, 992–8.

106. Karim B, Gupta D. (2014). Cheiloscopy & Blood groups: Aid in forensic identification. *Saudi Dental Journal*, 26,176–80.

107. Jain A, Bhaskar DJ, Gupta D, Yadav P, Khurana R. (2016). Practice of Self Medication for dental problems among residents of Uttar Pradesh, India. Oral Health Preventive Dentistry, 14, 5–11.

108. Jain A, Gupta D, Singh D, Garg Y, Saxena A, Chaudhary H. (2015). Knowledge regarding prescription of drugs among dental students: A descriptive study. *J Basic Clin Pharm.*, 7, 12–6.

109. Jain A, Bhaskar DJ, Gupta D, Agali C, Gupta V, Karim B. (2015). Comparative Evaluation of Honey, Chlorhexidine Gluconate (0.2%) and Combination of Xylitol and Chlorhexidine Mouthwash (0.2%) on the Clinical Level of Dental Plaque-A 30 Days Randomized Control Trial. Perspectives in Clinical Research, 6, 53–7.

110. Karim B, Bhaskar DJ, Agali C, Gupta D, Gupta RK, Jain A. (2013). Effect of *Aloe vera* Mouthwash on Periodontal Health: Triple Blind Randomized Control Trial. *Oral Health Dental Management*, 12, 1–6.