Aloe vera in Oral Diseases: Move toward the Nature

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ABSTRACT

The Egyptians called Aloe vera the "plant of immortality" because it can live and even flourish without soil. Aloe vera is well known for its spectacular medicinal properties. These plants are one of the richest sources of health for human beings provided by nature. It has been cultivated as an ornamental plant in different parts of the world. Products of the plant are used in the treatment of lot of medical problems. Aloe vera is gaining popularity in dentistry as it is completely natural and there are no side effects being reported with its use. It can be used in dentistry for its properties like wound-healing, gingivitis, plaque control, and treatment of oral mucosal lesions. Aloe vera may also reduce the pain and duration of oral ulcers as well as increase the rate of healing. It should be used by dentists at a high level in order to obtain maximum therapeutic advantage. This article gives an overview of the uses of this miracle plant in oral diseases.

Keywords: Aloe vera, Aphthous stomatitis, Oral diseases, Oral lichen planus, Oral submucous fibrosis


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INTRODUCTION

The concept of alternative medicine is currently on the rise in developing countries due to the World Health Organization efforts for the establishment of the scientific basis for the efficacy of many plants used in traditional medicine to treat infections. Aloe vera (A. vera) is a medicinal plant that belongs to the Liliaceae family. It is a cactus-like plant that grows commonly in hot tropical climates. The slimy gel in the A. vera leaf (A. vera gel) has been used for the treatment of the digestive tract disturbances, sunburn, and wounds.

The gel consists of 98 to 99% water while the remaining 1 to 2% contains the active compounds, such as aloeem, aloin, aloemodin, aloemannan, nafraquinones, methylchromones, flavonoids, saponin, sterols, amino acids, and vitamins. The levels of these components vary according to species, strain, and growth conditions. Aloe vera gel as studied acts as an anti-inflammatory, antibacterial, antioxidant, immune-boosting, and hypoglycemic agent.

The Aloe barbadensis plant consists of two different parts, each of which produces substances with completely different compositions and different therapeutic properties. The parenchymal tissue forms the inner portion of the A. vera leaves and produces the A. vera gel in the form of a clear, thin, tasteless, jelly-like material. This tissue is recovered from the leaf by separating the gel from the inner cellular remains. Pericyclic tubules are a group of specialized cells that form the other part of the plant. These cells occur just beneath the outer green ring of the leaf and produce an exudate that consists of bitter yellow latex with powerful laxative-like actions.

Aloe vera has been used in various systemic conditions like patients with skin disorders, bowel disorders, diabetes, and hyperlipidemia. It has also been used in dentistry for its useful properties in various conditions like lichen planus, aphthous stomatitis, oral submucous fibrosis, prevention of dry sockets, obturation of primary teeth, disinfection of irrigation solutions, bleeding and painful gums, disinfection of gutta-percha cones, burning mouth syndrome, and head and neck cancer patients undergoing the radiotherapy.

Proper diagnosis, knowledge of the traditional medicine, and implementation of that knowledge to the treatment plan are the important aspects for achieving success in the form of successful dental therapeutic agent. Aloe vera has a lot to offer in the field of dentistry. Various studies are being carried out to utilize the effective antimicrobial property of this miracle plant. A lot of interests are there for the use of A. vera in dentistry, and this natural therapy has already proved its unlimited use in our field. Standardization and quality assurance of A. vera products is a key area, which needs to be focused. Aloe vera is a promising herb with its various clinical applications in oral diseases.
HISTORY AND BACKGROUND

Ebers Papyrus in 1550 BC stated that 12 recipes were used for mixing Aloe with other agents to treat human disorders in Egyptian queens Cleopatra and Nefertiti. Aloe vera was given importance by both queens as being an important donor to their beauty. It was traded on a large scale in the Near East and Asia in 400 BC. Alexander the Great in 333 BC captured the Island of Socotra because of its aloe supplies. Later Dioscorides wrote a detailed description of A. vera and all of its uses in 68 AD. In 200 AD, A. vera became an important part of Roman medicine and got extremely popular in Europe. In 1500 AD, it was introduced to the world by the conquistadors. In 1655, John Goodyew mentioned about A. vera in his book “Dioscorides Medical Treatise De Materia Medic.” In 1934, A. vera was published for the first time in the modern medical paper. It mentioned how the whole leaf was used to treat radiation dermatitis. Various papers were published in the 20th century describing a wide range of medicinal properties.

MECHANISM OF ACTION

Aloe vera contains several active constituents: Vitamins, enzymes, minerals, sugars, saponins, salicylic acids, and amino acids. Aloe vera is a potent anti-inflammatory agent; it inhibits the Cyclooxygenase (CXO) pathway and reduces prostaglandin E2 production from arachidonic acid. It has penetrating capacity to reach deeper layers of the dermis when applied topically. It has strong antiseptic properties mainly bactericidal, fungicidal, and virucidal. It has the ability to promote cell growth. Aloe vera has the neurological mechanism to produce the antianxiety effect. Besides, it can also act as a detoxifying agent. It enhances defense mechanisms and helps to fight against periodontal disease and other oral conditions.

ALOE VERA AND SYSTEMIC HEALTH

Wound-healing Effects

Several mechanisms have been proposed for the wound-healing effects of Aloe gel, which include keeping the wound moist, increasing epithelial cell migration, more rapid maturation of collagen, and reduction in inflammation. A study reported that a high molecular weight polypeptide constituent of the A. vera gel showed a healing effect on excisional wounds in rats. Glucomannan, a mannose-rich polysaccharide, and gibberellin, a growth hormone, interact with growth factor receptor on the fibroblast, and increase its activity and proliferation, which further increases collagen synthesis after topical and oral application. Polysaccharides isolated from A. vera induce matrix metalloproteidase (MMP)-3 and metalloproteidase inhibitor-2 gene expression during the skin wound repair of rat, which directly helps to regulate the wound-healing activity of A. vera gel.

Immunomodulating Effects

Aloe vera contains 90% rhodium and iridium (trace minerals) in the acemannan, which is one of the polysaccharides having a role in increasing the white blood cells and acts as a great immune activator, or macrophages and T cells. Thus, immunomodulating effects occur via activation of macrophage cells to generate nitric oxide, cytokines like tumor necrosis factor, interleukin-1, interleukin-6, and interferon-gamma, and present cell surface markers. It plays an important role in the enlargement of the thymus gland in size by 40%. The thymus produces the T cells of the immune system. A recent report of a clinical study evaluated the therapeutic effect of A. vera gel, wherein 2% oral gel is not only effective in decreasing the pain and wound size in recurrent aphthous stomatitis patients but also actively decrease the aphthous wound-healing period.

Property as Antioxidant

Aloe vera has very strong antioxidant nutrients. Glutathione peroxide activity, superoxide dismutase enzymes, and a phenolic antioxidant are found in A. vera gel, which may be responsible for these antioxidant effects. Besides it also contains vitamins A, C, and E. These free radical components play a key role in the reduction of the toxins and carcinogenic products, which are present in our bodies from the pollution and poor quality foods. These free radicals are acquired in our bodies through absorption of our skin and digestion. The extracts of leaf skins and flowers of A. vera were also evaluated for their antioxidant and antimycoplasmic activities, and in vitro antioxidant activities of both extracts demonstrated antioxidant activity, with the leaf skin extract being the most active.

Antitumor Effect

The two constituents from A. vera that are found to have anticancer effects include glycoproteins (lectins) and polysaccharides. Many studies showed antitumor activity for A. vera gel in terms of reduced tumor burden, tumor shrinkage, tumor necrosis, and prolonged survival rates. An induction of glutathione S-transferase and an inhibition of the tumor-promoting effect of phorbolmyristic acetate have also been reported, which suggest Aloe gel in cancer chemoprevention. Indirect action on antitumor activity is through stimulation of the immune response. Aloin, an anthraquinone which is a natural compound.
and the main ingredient of Aloe, has been reviewed for its extraordinary potential therapeutic options in cancer, wherein it showed chemoprotective effects against 1,2-dimethylhydrazine-induced preneoplastic lesions in the colon of Wistar rats.13

Anti-inflammatory Effects

It inhibits the CXO pathway and reduces prostaglandin E2. Recently, C-glucosylchromone, a novel anti-inflammatory compound, has been isolated from gel extracts. In addition, the peptidase brady kinase has been isolated from Aloe which causes breakdown of the bradykinin, an inflammatory substance that induces pain. The topical anti-inflammatory activity of A. vera was evaluated by Davis using croton oil-induced edema assay and found that small amounts of A. vera given topically should inhibit inflammation. Aloe vera inhibits the cyclogease pathway and reduces prostaglandin E2 production from arachidonic acid. Recently, the novel anti-inflammatory compound called C-glucosylchromone was isolated from gel extracts.14

Antibacterial Property and Antifungal Property

The effect of A. vera inner gel against both Gram-positive and Gram-negative bacteria has been observed. Strep-tococcus pyogenes and Streptococcus faecalis have been inhibited by A. vera gel. The bactericidal action against Pseudomonas aeruginosa also has been found. A processed A. vera gel preparation reportedly inhibited the growth of Candida albicans. It has been demonstrated by a recent study that the A. vera inner gel shows antibacterial properties against both susceptible and resistant Helicobacter pylori strains and the effect on the antimicrobial resistance phenomenon of H. pylori. The A. vera inner gel is an effective natural agent for combination with antibiotics for the treatment of H. pylori infection.

Antiviral Property

Many reports have suggested that the anthraquinones acts like tetracycline that inhibits bacterial protein synthesis by blocking the ribosomal A site. Therefore, in the media containing A. vera extract, the bacteria is unable to grow. An in vitro study has concluded that crude extract of A. vera gel is active against herpes simplex virus type 2 strain. Anthraquinone derivatives have been found to have antiviral activity. They are believed to have inhibitory mechanism against influenza A virus by reducing virus-induced cytopathic effect and preventing replication of influenza A. The experiment was helpful in demonstrating that A. vera was capable of expressing a human protein with its biological activity, namely interferon-alpha 2.15

Antidiabetic Effect

Clinical studies have suggested that A. vera gel may act as a useful antihyperglycemic and antihypercholesterolemic agent for type 2 diabetic patients without any significant effects on other normal blood lipid levels or liver/kidney function.16 In a randomized controlled trial, A. vera gel complex significantly reduced body weight, body fat mass, and insulin resistance in obese prediabetes and early nontreated diabetic patients. Further, in a pilot study, two A. vera products in patients with prediabetes were found to rectify the impaired fasting glucose and impaired glucose tolerance observed in conditions of prediabetes/metabolic syndrome.17

Hepatoprotective Effect

It has been demonstrated that isolated phytosterols, namely lphenol and cycloartanol, have the ability to induce the downregulation of fatty acid synthesis. Besides they have a tendency for upregulation of fatty acid oxidation in the liver, which lead to the reduction in intra-abdominal fat and improvement of hyperlipidemia. Further, on addition of sterol regulatory element-binding protein, the transcription factor 1/peroxisome proliferator-activated receptor (PPAR)-α ratio decreased; metabolic syndrome-related disorders and liver steatosis improved in Aloe vera–sterol-treated Zucker diabetic fatty rats.18 The combination of probiotic Lactobacillus rhamnosus GG and A. vera gel has been found to have a therapeutic potential to decrease cholesterol levels and the risk of cardiovascular diseases.19

Antihyperlipidemic Activity and Weight Control

It helps to reduce the development of atherosclerosis through modification of risk factors due to its antihyperlipidemic property. The efficacy of A. vera leaf gel has been checked in hyperlipidemic type 2 diabetic patients by a randomized double-blind placebo-controlled clinical trial, wherein total cholesterol and LDL levels were significantly reduced.16 A recent study also demonstrated that administration of phytosterols isolated from visceral fat mass is reduced and hyperglycemia is improved by A. vera gel.20

Intestinal Absorption

Aloe vera material has been used for drug absorption in drugs with low bioavailability.21 Lactobacillus brevis strains have been isolated from naturally fermented A. vera gel which inhibited the growth of many harmful enteropathogens without affecting most normal commensals in the gut and hence were named probiotics originating from Aloe leaf (POAL) strains. They exhibit
discriminative resistance to a wide range of antibiotics.\textsuperscript{22} Aloin, present in the gel, is metabolized by the colonic flora to active Aloe-emodin, which is responsible for the purgative activity. Isolation of Aloe-emodin from \textit{A. vera} inhibits colon cancer cell migration by downregulating MMP-2/9 via reducing DNA binding activity of nuclear factor kappa-light-chain-enhancer of activated B cells.\textsuperscript{23}

**VARIOUS FORMS OF ALOE VERA USED**

\textit{Aloe vera} is used in the form of a toothpaste or mouthwash. It can be used as gel for promoting healing in burns, stings, insect bites, and many skin lesions where it protects and promotes healing. Another form of use is \textit{Aloe} activator topical spray, which is used for throat infections, painful teeth eruptions, and joint pains. Further, \textit{A. vera} juice is taken systemically as a drink for irritable bowel syndrome and as a strong detoxifying agent. It also acts as neurosedative, an immune enhancer, as powerful nutritional supplement, and antioxidant.\textsuperscript{24,25}

**ALOE VERA IN ORAL HEALTH**

**Aphthous Stomatitis**

\textit{Aloe vera} oral gel is effective in decreasing the recurrent aphthous stomatitis patient's pain score and wound size as well as decreases the aphthous wound-healing period.\textsuperscript{26} Acute mouth lesions are improved by direct application of gel on herpetic viral lesions or aphthous ulcers. It has been reported that acemannan hydrogel accelerates the healing of aphthous ulcers as well as reduces the pain associated with them.\textsuperscript{27} Acemannan, which is one of the polysaccharide components in \textit{A. vera}, has been used for the treatment of oral aphthous ulceration in patients, generally, who didn't want steroid medication. US Food and Drug Administration has also found a derivative of \textit{A. vera} as an effective treatment alternative in treating oral ulcers.\textsuperscript{26}

In a study conducted by Babae et al\textsuperscript{11} on 40 patients of minor recurrent aphthous stomatitis, \textit{A. vera} gel was found effective in reducing the intensity of pain as well as reduced the healing time of less than 7 days. Several other studies have been carried out to show effectiveness of the anti-inflammatory and wound-healing properties of \textit{A. vera} gel in retinoic acid syndrome patients.

**Oral Lichen Planus**

Treatment of lichen planus has also been done using \textit{A. vera}. The severity of the oral lesions and the oral quality of life of the patients with Oral Lichen Planus (OLP) improved if applied topically 3 times a day. Several studies have reported that \textit{A. vera} can be used in dosages of two ounces of \textit{A. vera} juice 3 times a day for 3 months.\textsuperscript{27} Steroids have remained the mainstay treatment modality in case of lichen planus; however, long-term steroids therapy can lead to multiple systemic complications. \textit{Aloe vera} has an added advantage due its lesser side effects. Topical \textit{A. vera} gave better results when compared with triamcinoline.\textsuperscript{26}

Choonhakarn et al\textsuperscript{28} conducted a study to know the efficacy of \textit{A. vera} gel in the treatment of OLP. A randomized, double-blind, placebo-controlled trial was designed in which fifty-four patients were divided into two groups to receive \textit{A. vera} gel or placebo for 8 weeks out of which 34 were women and 20 were men. Twenty two of 27 patients treated with \textit{A. vera} (81\%) had a good response after 8 weeks of treatment. Burning pain completely disappeared in nine patients treated with \textit{A. vera} (33\%). Symptomatology improved by at least 50\% (good response) in 17 patients treated with \textit{A. vera} (63\%). Both groups did not show any serious side effects. In inducing clinical and symptomatological improvement of OLP, \textit{A. vera} gel was statistically significantly more effective than placebo. Therefore, it was concluded that \textit{A. vera} gel could be considered as a safe alternative treatment for patients with OLP.

**Oral Submucous Fibrosis**

A preliminary study was carried out to compare the efficacy of \textit{A. vera} with antioxidants in the treatment of Oral Submucous Fibrosis (OSMF).\textsuperscript{29} In this study, 20 subjects with OSMF were included. The patients are divided into two groups: Group A received 5 mg of \textit{A. vera} gel three times daily for 3 months, and group B received antioxidant capsules twice daily for 3 months. It was concluded that \textit{A. vera} group had a better treatment response than the antioxidants group. Hence for the treatment of OSMF, it can be applied topically and effective.

Alam et al\textsuperscript{30} conducted a double-blind, placebo-controlled, parallel-group randomized controlled trial on 60 subjects with OSMF. The patients were divided into medicinal treatment (submucosal injection of hyalurondase and dexamethasone, \textit{n} = 30) and surgical treatment (\textit{n} = 30) categories. Both the categories were randomly divided into group A (with \textit{A. vera}) and group B (without \textit{A. vera}), \textit{n} = 15 per category. For various symptoms, follow-up assessment was performed, and the analysis of result was done using paired and unpaired Student’s \textit{t}-tests. It was concluded that the group receiving \textit{A. vera} had a significant improvement in most symptoms of OSMF (\textit{p} < 0.01) as compared with the non-aloe vera group.

**Oral Leukoplakia**

\textit{Aloe vera} has very strong antioxidant nutrients. It was found that glutathione peroxide activity, superoxide dismutase enzymes, and a phenolic antioxidant were
Aloe Vera in Oral Diseases: Move toward the Nature

present in *A. vera* gel, which may be responsible for these antioxidant effects. Along with these, it also has vitamins A, C, and E. These free radical components play key role in removing the toxins and carcinogens we have in our bodies from the pollution and poor quality foods. Free radicals are acquired in our bodies through absorption of our skin and digestion. *Aloe vera* has its action on the reduction of tumor cells. There are several active components responsible for antioxidant nature of *A. vera*. There are other important properties of *A. vera* like immunomodulator property. Based on these properties, *A. vera* gel can be used in the treatment of oral leukoplakia. 

**Radiation-induced Oral Mucositis**

Ahmadi 31 conducted a study and demonstrated that oral *A. vera* mouthwash can be used effectively in radiation-induced mucositis by virtue of its wound healing and anti-inflammatory mechanism. It also reduces oral candidiasis of patients undergoing head and neck radiotherapy due to its antifungal and immunomodulatory properties. Hence, *A. vera* mouthwash is an alternative agent for treating radiation-induced oral mucositis and candidiasis in patients with head and neck cancers. Immunomodulating effects occur via activation of macrophage cells to generate nitric oxide, cytokines like tumor necrosis factor, interleukin-1, interleukin-6, and interferon-gamma, and present cell surface markers. It plays an important role in the enlargement of the thymus gland in size by 40%. The thymus produces the T cells of the immune system. All these properties help in treating the radiation-induced oral mucositis.

**Gingivitis**

A study was conducted by Ajmera et al32 to evaluate the anti-inflammatory property of *A. vera* mouthwash on plaque-induced gingivitis. Forty-five patients who were diagnosed with plaque-induced gingivitis were included in the study. All these patients were divided into three groups with 15 patients in each group. Group 1 rinsed with 10 mL of *A. vera* mouthwash twice daily for 3 months. Group 2 were treated with scaling and root planing (SRP) only. Group 3 patients were asked to rinse with *A. vera* mouthwash and scaling was done. The result suggested reduction in gingival inflammation in all the three groups, but it was found that the response was better in the *A. vera* mouthwash and scaling group. Davis et al.33 conducted a study to demonstrate the anti-inflammatory and wound-healing activity of *A. vera* due to the presence of growth substance mannose-6 phosphate. Hence, it was stated that *A. vera* had a significant anti-inflammatory property. Thus, it can be used along with the mechanical therapy for treating plaque-induced gingivitis. Bovik34 conducted a research where he used *A. vera* for the gingivectomy sites and it was found that healing was better and fast.

**Periodontitis**

Bhat et al35 conducted a trial to demonstrate the clinical effects of subgingival application of *A. vera* gel in periodontal pockets patients after mechanical debridement. In this study, 15 subjects were examined for clinical parameters, such as, plaque index, gingival index, probing pocket depth, followed by SRP. The method of evaluation consisted of SRP, followed by intrapocket placement of *A. vera* gel, which was compared with the control site in which only SRP was done, and the clinical parameters were compared between the two sites at 1 and 3 months. Results of the study demonstrated better response in clinical parameters where *A. vera* gel was used as a drug for local delivery. Based on these results, it was concluded that subgingival administration of *A. vera* gel results in improvement of periodontal condition. In conclusion, *A. vera* gel can be used as a local drug delivery system successfully in periodontal pockets with better results.

**Antihersensitivity Action**

*Aloe vera* tooth gel is effective in controlling bacteria that causes cavities than other commercially available toothpaste. *Aloe vera* gel’s ability to kill microorganisms is due to compounds called anthraquinones, which are anti-inflammatory. *Aloe vera* gel does not contain the abrasives found in most toothpastes; hence the possibility of regressive changes of teeth is quite low. In addition, it is a better alternative for people with sensitive teeth. George et al36 conducted an *in vitro* study to demonstrate the antimicrobial activity of an *A. vera* tooth gel and two commercially popular toothpastes and concluded that *A. vera* tooth gel was effective than two commercially popular toothpastes in controlling all the organisms like, *Streptococcus mutans, C. albicans, S. mitis, Enterococcus faecalis, Prevotella intermedia*.38 Also, the *A. vera* gel demonstrated better antibacterial effect against *Streptococcus mitis* despite the absence of additional fluoride.37

**Alveolar Osteitis**

Poor et al38 compared the cases of Alveolar Osteitis (AO) in patients treated with either clindamycin-soaked Gelfoam or SaliCept Patches being prepared using *A. vera* gel. The SaliCept Patch used is a freeze-dried pledget that contains acemannan hydrogel obtained from the gel of *A. vera*. The results showed that the SaliCept Patch reduced the incidence of AO as compared with clindamycin-
soaked Gelfoam. The anthraquinones acts like tetracycline that inhibits bacterial protein synthesis by blocking the ribosomal A site. Habeeb and Shakir carried out a study and demonstrated the effectiveness of A. vera gel against Gram-positive as well as Gram-negative bacteria.39

**Fungal Infections of Oral Cavity**

Oral fungal infections are opportunistic infections. These are chronic and omnipresent in nature. They have a slow rate of progression and are often asymptomatic for large number of years. When their growth is significantly large, then the problem arises. But, usually by then the, problem has reached a sufficient intensity that it becomes very difficult to treat and remove it completely. The problem of recurrence is very common with Candida infection. The problem is aggravated with the increase in the growth of the resistance of the organism to the antifungal medication. Aloe vera is now gaining popularity in the field of dental medicine. Several studies demonstrated that the gel has a potent antifungal activity. This is in agreement with the studies done by George et al.36. The activity increases with the increase in the dose. This is also in agreement with the studies done by Heggers et al.40

**Viral Infections**

This action may be direct or indirect: The action may be indirect due to stimulation of immune system, and direct due to Aloe-emodin. Aloe-emodin in A. vera has been found out to act against virus replication. Therefore, A. vera is virucidal to herpes simplex virus type 1 and type 2, varicella zoster virus, pseudorabies virus, and influenza virus according to the research of Thomson. Hence, A. vera can be used for treating herpes labialis, herpes zoster, and other viral infection of oral cavity. It has been found after several studies that the virucidal activity was due to the anthraquinones. This is obtained by extracting from the inner leaf of Aloe and the roots, bark, or leaves of a number of other anthraquinone containing plants. The results showed that both DNA- and RNA-containing enveloped viruses were directly affected by Aloe-emodin but had no effect on naked one.5

**ADVANTAGES, DISADVANTAGES, DRUG INTERACTIONS**

*Aloe vera* can be used as a local drug delivery system because of its various benefits. It is easily applicable with minimal equipments. *Aloe vera* products are cost effective. Their major advantage is presence of least adverse effects.

It is contraindicated in cases of known allergy to plants in the Liliaceae family, pregnancy and breastfeeding.

Oral *A. vera* is not recommended during pregnancy due to theoretical stimulation of uterine contractions, and in breastfeeding mothers, it may sometime cause gastrointestinal distress in the nursing infant.35

Application of Aloe to the skin may increase the absorption of steroid creams like hydrocortisone. It may increase the adverse effects of digoxin and digitoxin, due to its potassium lowering effect. Use of both *A. vera* and furosemide may increase the risk of potassium depletion. The blood sugar levels are reduced and thus interaction with oral hypoglycemic drugs and insulin may occur.5

**CONCLUSION**

In contrast with traditional medicine modalities, *A. vera* is quite economical and has almost no side effects. Both medical cost and invalidity will be reduced. Dentistry is changing with induction of alternative medicine like *A. vera*. But considerable amount of literature is not available relating to the use of *A. vera* in oral diseases. Hence, more studies are required with larger sample size in this regard. To know the healing properties, antibacterial, anti-inflammatory properties, and releasing pattern as a local drug delivery system, more researches are required.

**REFERENCES**


