Case Series

Evaluating the efficacy of pumpkin seed extract as a local drug deliver agent in chronic periodontitis patients: A case series

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ABSTRACT

Background: To assess the efficacy of pumpkin seed extract as a local drug delivery agent (LDD) in the management of deep periodontal pockets. **Materials and methods:** In the current study, the effectiveness of a locally developed gel formulation of pumpkin seed extract as an adjuvant in the management of chronic periodontitis is assessed. There were eight patients with a total of ten sites with localised periodontal disease and a pocket probing depth (PPD) of more than five millimetres. As part of the routine periodontal treatment procedure, all patients received professional oral prophylaxis and root planing. The produced extract was injected subgingivally two weeks after prophylaxis. At baseline, 15 days, one month, and three months, clinical parameters such the plaque index (PI), gingival index (GI), PPD, and clinical attachment level (CAL) were noted.**Results:** All the assessed clinical parameters showed considerable improvement when compared to the baseline values. The obtained values were statistically significant with the p-value <0.0001. **Conclusion:** Pumpkin seed extract is an effective phytotherapeutic agent that can be used as adjunct to scaling and root planning to reduce the PPD and inflammatory state of the periodontium.

Key words:Chronic Periodontitis, Local Drug Delivery, Periodontal Pocket, Pumpkin Seed Extracts

Periodontal diseases are conditions that affect the periodontium, the word used to refer to the framework that supports the tooth and is made up of the gingiva, alveolar bone, cementum, and periodontal ligament. When oral hygiene is improved, the reactive condition of gingivitis can be reversed. Periodontitis is a persistent, damaging, and permanent inflammatory disease state that results when the periodontal problem has advanced past gingivitis. The microorganisms can then enter the tissues and surrounding periodontium more deeply. As a result, the host reacts in an effort to fight off the invasive bacteria. Unfortunately, the host defences also cause the periodontium to be destroyed when defending against the bacteria. [1]

The advanced type of periodontal disease is defined by the breakdown of the alveolar bone around the periodontium and the loss of periodontal ligaments. It is regarded as one of the two greatest risks to oral health and the primary cause of tooth loss. In the mouth cavity, there are over 800 different species of bacteria, and it is thought that a complicated interaction between bacterial infection and human defence, influenced by behavioural factors like smoking, can lead to periodontal disease. [2]

The gingival sulcus refers to the anatomical space that exists between the tooth's neck and the surrounding gingival tissue. There is a shallow gingival sulcus surrounding teeth in a clinically healthy setting (0 to 3 mm depth). When this shallow cleft widens due to apical migration of junctional epithelium and attachment loss as a result of the periodontal disease process, it is known as the creation of a pathologically deepened pocket or periodontal pocket. In this case, the gingival sulcus transforms into a periodontal pocket where the depth of the sulcus becomes greater than three mm. [3]

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There are various treatment strategies to reduce the periodontal probing pocket depth (PPD).The treatment involves non-surgical phase where scaling, root planning, and local drug delivery are administered. If the PPD does not resolve after non-surgical periodontal therapy, the surgical therapy is pursued. Local drug delivery (LDD) is a preferred treatment option for isolated pocket reduction and to reduce the inflammatory response in that particular region. Over the years various medications have been attempted as LDD. The most popular drug in this category is tetracycline derivatives. However, concerns over antibiotic resistance, and lack of awareness among the patients regarding the adverse effects has led a way to employ natural herbs as LDD agents. [4]The Cucurbitaceae family includes pumpkins. Due to its high nutrient content, pumpkin (Cucurbitamoschata), one of the most popular vegetables consumed worldwide, has been manufactured as food. According to recent studies, pumpkin has a number of bioactive components that are anti-diabetic, anti-inflammation, anti-cancer, etc. Moreover, pumpkin seeds (PS) are a good source of protein and fat and have advantageous health effects. Its secondary metabolite extracts are useful for immunomodulation, reproductive health, and treatments across a wide range of clinical circumstances. They can also accelerate the metabolism of stored lipids. [5, 6]

Many studies have found that PS oil can lower blood lipid levels and treat metabolic disorders, and another found that pumpkin's protein-bound polysaccharide can delay the onset of type I diabetes. Moreover, the combined effects of phytosterols, -6 and -9 unsaturated fatty acids (UFA), total phenolics, beta-carotene, etc. may be responsible for PS oil's anti-inflammatory activity. [7] Vanillic acid can be found in abundance in PSs. Plants produce vanillic acid as a byproduct of secondary metabolism (4-hydroxy-3-methoxy benzoic acid). It is frequently utilised in fragrance, as a food additive, and as a preservative. In addition to its potent antioxidant effects, vanillic acid also has hypotensive, cardioprotective, hepatoprotective, antiapoptotic, and even gene regulatory functions. [8, 9]Considering the above-mentioned advantages, a study was done to assess the anti-inflammatory efficiency of PS extract in the form of LDD mixed in a biodegradable gel for the treatment of periodontal pockets.

MATERIALS AND METHODS

The present interventional study was conducted after the approval by Institutional Ethical Committee. This study was designed to evaluate the use of an indigenously prepared PS extract gel, as an adjunctive targeted drug therapy in the management of periodontal pockets. The study design comprised of an introducing the prepared gel into deep periodontal pockets measuring >5 mm.

Extraction of pumpkin seed oil

PSs were manually extracted from the shells and washed thoroughly to get rid of foreign objects or unnecessary pollutants like trash, plant bits, and damaged seeds. The seeds were first sun dried for 3 days and later oven dried at 150 °C for three hours. The samples were then calculated for the probable mass loss from evaporation as a result of the drying.

A stoppered jar containing 50 grammes of coarsely powdered PSs was filled with 100% alcohol and left in place for five days with continuous stirring. The solvent was then evaporated in a hoover evaporator, i.e., Rota evaporator, after that. After pressing the mixture, a gravimetric analysis determined that the oil yield was 9%. This method's oil was accepted as the entirety of PS's oil content. An investigation by Pappu R et al. in 2019 mentioned a similar technique for extracting flax seed oil. [10] The subsequent phase required creating a gel version of a PS extract for simplicity of use as a LDD agent. A 1:1 ratio of polymer to PS oil was used. In order to achieve a uniform dispersion in the form of a gel, 200 mg of carbopol polymer was added to 200 mg of PS oil extract in a glass vial. The vial was then sonicated and LDD dispersion syringe was prepared from the same.

The drug was then introduced into ten isolated PPD with a probing depth > 5mm in patients who were systemically healthy, non-smoker individuals, and above 35 years of age. Patients were excluded if they were pregnant and lactating mothers, below <35 years of age, presence of smoking habit or any other debilitating disease, generalized PPD. After excluding the patients based on the above-mentioned criteria, eight patients with ten isolated pockets in ten quadrants were included for the study. Scaling and root planing, along with oral hygiene instructions, were the non-surgical periodontal therapy that was given to those who expressed a willingness to participate and gave written informed consent. After two weeks, the patients were recalled and PPD were reassessed. For the intervention, only those with persistent PPD were chosen. To ensure reproducibility at each visit and to standardise the placement of the probe into the pockets, occlusal stents were prepared. Plaque index (PI), gingival index (GI), PPD, and clinical attachment level (CAL) were all documented at baseline. A syringe and needle were used to carefully administer 0.2 mL of the produced extract after isolating the test site. When this gel comes in contact with the gingival epithelium, it has a

tendency to solidify into a matrix.The patients were then reinforced with oral hygiene instructions and recalled after 15 days, 30 days and at 3rd month for re-evaluation of PI, GI, PPD and CAL.

Statistical analysis

The measured values of the clinical parameters were examined using statistical software (SPSS version 20, IBM). To compare the preoperative and postoperative data, a repeated-measures ANOVA with post hoc Bonferroni test was utilised. Statistical significance was defined as a p-value< 0.001.

RESULTS

The experimental local drug was administered to eight patients across a total of ten sites. After three months of observation, every location had successfully recovered. There were no side effects or allergic reactions that might have been brought on by the experimental treatment modalities. The mean plaque index, gingival index, sulcus bleeding index, probing pocket depth, as well as a statistically significant increase in clinical attachment from baseline, were all statistically significantly lower in the current study. The details of the study results are highlighted in table 1.

Table 1: Evaluation of the clinical parameters at baseline and post-introduction of LDD at 15, 30, and 90 days.

	Values		P-value	Post-hoc test
	Mean	SD		
PPD base	6.10	.15	<0.001	B>15,30, 90
PPD 15 days	2.02	.24		
PPD 30 days	1.01	.31		
PPD 90 days	1.14	.22		
CAL base	7.23	.63	<0.001	B>15, 30, 90
CAL 15 days	3.03	.15		
CAL 30 days	3.16	.43		
CAL 90 days	3.42	.03		
GI base	2.75	0.32	<0.001	B> 15, 30, 90
GI 15 days	0.79	0.18		
GI 30 days	0.46	1.17		
GI 90 days	0.49	0.32		

DISCUSSION

A range of chemotherapeutic drugs are effective against potential periodontal disease bacteria. As an adjunct to SRP, these medications can be applied topically or systemically in an effort to further decrease the quantity of periodontal bacteria and consequently improve the periodontal condition. LDD of antimicrobial and anti-inflammatory drugs has been the subject of in-depth study in recent years. The present study employed PS oil infused in a polymer to treat PPD. To best of our knowledge, this is the first interventional study to use PS extract to combat periodontal destruction and host inflammatory response. [11] For periodontal healing, potential periodontopathic microorganisms in the subgingivalmicrobiota must be eliminated or sufficiently suppressed. The antibiotic must penetrate the depth of the pocket and result in gingival fluid concentrations greater than the minimum inhibitory concentrations (MIC) of the suspected bacteria for the treatment to be effective. [12]

Periodontal pockets have been successfully treated with systemic medication, however frequent and prolonged use of systemic antibiotics carries a risk of superimposed infections and resistant strains. Hence, local government offers a helpful solution to these issues. The primary condition for this type of therapy to be effective is that the agent enters the pocket and is kept there using a reservoir long enough for the antibacterial effect to take place. [13] Dr. Max Goodson et al's proposal for the use of controlled delivery in the management of periodontitis was made in the year 1979. [14] The use of allopathic drugs as LDD systems works well. Ayurvedic and herbal medicines are becoming more and more popular recently as a way to get beyond the limitations of allopathic medicine. 2011 saw a rise in the usage of herbal remedies as LDD agents; the many available are Neem, Aloe-vera, Lemon-grass, Green Tea, Tea Tree Oil, Curcumin, Oak, Coriander, Babul, and Bakul. [15]

Few of the examples for herbal products working effectively in subgingival environment are as follows. Aloe vera showed antibacterial action against periodontal pathogens, according to Jain J's 2016 investigation into the antibacterial impact of aloevera gel against oral pathogens, and he indicated that it might be employed as an LDD system in periodontal pockets. [16]In a study by Warad SB et al. (2013) [48] 2% lemongrass oil in gel form was locally administered to PPD> 5mm, and it was discovered that this alternative to SRP is both secure and efficient. [17] SRP alone versus in combination with green tea catechins as LDD into periodontal pockets were examined in a randomized, placebo-controlled split mouth trial by Hattarki SA et al (2013)[52]. This study revealed that green tea was more effective than SRP alone. [18]

According to Nagasri M. (2013) [56], individuals with chronic periodontitis benefit from the local use of curcumin combined with SRP due to improvements in periodontal parameters. [19] Similar to the above-mentioned studies that employed herbal based products to

counteract the inflammatory process in the subgingival environment, the present study employed PS extract as a LDD in areas of PPD>5mm. From low elevations to high altitudes, pumpkin can be grown as an annual vine or trailing plant. It is renowned for its eatable fruit, nuts, and greens. The low-fat and protein-rich seeds of the pumpkin are its most significant component. [20] Many chronic systemic inflammatory disorders have been linked to oxidative stress. [21] Several pumpkin extracts show significant antioxidant activity that could be crucial in decreasing inflammation. Vitamin E is abundant in PSs, and PS oil is thought to be an important source of vitamin E in Japanese diets. Also, it was discovered that pumpkin polysaccharide might raise glutathione peroxidase and superoxide dismutase activity and lower malonaldehyde levels in tumor-containing mouse blood. [22]

CONCLUSION

For its nutritional and therapeutic benefits in the treatment of many illnesses and inflammatory diseases, pumpkin seed oil has been used as a food ingredient for a long time. As a supplement to SRP in the current study, pumpkin seed extract was employed, and the results show that the GI, PPD, and CAL decreased at a statistically significant level. To the best of our knowledge, this trial is the first to use subgingival administration of pumpkin seed extract in conjunction with SRP to treat PPD.

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