

## Original Research Article

### The Effectiveness of Acacia Arabica Gum as an adjunct to The Non-Surgical Treatment of Chronic Periodontitis

#### Abstract

**Comment [u1]:** Please, show the aims of your study

In the presented study the pharmacological effect of Acacia Arabic gum was estimated in A hospital based double blinded, randomized clinical trial using split mouth technique, conducted in the *Khartoum Dental Teaching Hospital (KDTH)*. All patients diagnosed with chronic periodontitis according to American Academy Periodontology. As *used* split mouth technique, 88 sites (44 scaling and root planning and gum *Arabic*) had been enrolled randomly as intervention group, (44 sites scaling and root planning + distilled water) as a *control group*. PI, GI, BOP, PPD, CAL, measurements and scores in addition to IL-1 $\beta$  was done *on* day 0 and day 30. (47.7%) of the study were males and (52.3%) were females with the mean age was 40.7 years  $\pm$ 12.7. **PI, GI, BOP, PPD, CAL and IL1 $\beta$**  measurements showed a significant reduction in the *AA group* ( $P < 0.05$ ). This study concludes that the adjunctive use of a pulsating jet containing AA as an irrigation solution was efficient in reducing plaque index, gingival index, and BOP, PPD, CAL, as well as IL 1 $\beta$  level in subjects with chronic periodontitis.

**Comment [u2]:** Please avoid abbreviation in abstract  
Gingival index(GI), bleeding on probing (BOP),pocket probing depth (PPD), clinical attachment loss (CAL) and interleukin 1(IL 1).

**Key words:** periodontitis, chronic periodontitis, Acacia Arabic, IL 1 $\beta$

**Comment [u3]:** At least 5 keywords must be written

#### 1. Introduction

##### 1.1 Periodontitis

Periodontal disease, also said as gum disease, is additionally a set of inflammatory conditions affecting the tissues surrounding the teeth <sup>[1]</sup>. In its early stage, called gingivitis, the gums become swollen, red, and can bleed <sup>[2]</sup>. In its more serious form, called periodontitis, the gums can regress from the tooth, bone is lost, and thus the teeth may loosen or fall out <sup>[3]</sup>. Bad breath may additionally occur <sup>[4]</sup>. Periodontal disease is typically thanks to bacteria within the mouth infecting the tissue round the teeth. Factors that increase the danger of disease include smoking, diabetes, HIV/AIDS, history, and certain medications. Diagnosis is by inspecting the gum tissue round the teeth both visually and with a glance and X-rays trying to look out bone loss round the teeth [. Treatment involves good oral hygiene and regular professional teeth

cleaning. Recommended oral hygiene include daily brushing and flossing. In certain cases, antibiotics or odontology could even be recommended. Globally 538 million people were estimated to be affected in 2015 <sup>[5]</sup>. within the u. s. nearly half those over the age of 30 are affected to some extent, and about 70% of these over 65 have the condition, males are affected more often than females <sup>[6]</sup>.

### 1.1.1 Signs and symptoms

In the early stages, periodontitis has just some symptoms, and in many individuals the disease has progressed significantly before they seek treatment.

#### 1.1.2 Symptoms may include

- Redness or bleeding of gums while brushing teeth, using floss or biting into hard food (e.g., apples) (though this may also occur in gingivitis, where there's no attachment loss)
- Gum swelling that recurs
- Spitting out blood after brushing teeth
- Halitosis, or bad breath, and a persistent metallic taste within the mouth
- Gingival recession, leading to apparent lengthening of teeth (this could even be caused by heavy-handed brushing or with a stiff toothbrush)
- Deep pockets between the teeth and also the gums (pockets are sites where the attachment has been gradually destroyed by collagen-destroying enzymes, called collagenases)
- Loose teeth, within the later stages (though this might occur for other reasons, as well) People should realize gingival inflammation and bone destruction are largely painless. Hence, people may wrongly assume painless bleeding after teeth cleaning is insignificant, although this might be a logo of progressing periodontitis therein person <sup>[5][6]</sup>.

### 1.1.3 Causes

Periodontitis is an inflammation of the periodontium, i.e., the tissues that support the teeth.

#### The periodontium consists of 4 tissues

- gingiva, or gum tissue,
- cementum, or outer layer of the roots of teeth,

- alveolar bone, or the bony sockets into which the teeth are anchored, and
- periodontal ligaments (PDLs), which are the tissue fibers that run between the cementum and also the alveolar bone.

The primary reason for gingivitis is poor or ineffective oral hygiene,<sup>[7]</sup> which finally ends up within the buildup of a mycotic<sup>[8][9][10][11]</sup> and bacterial matrix at the gum line, called plaque. Other contributors are poor nutrition and underlying medical issues like diabetes<sup>[12]</sup>. Diabetics must be meticulous with their homecare to manage disease<sup>[13]</sup>. New finger prick tests are approved by the Food and Drug Administration within the US, and have gotten utilized in dental offices to identify and screen people for possible contributory causes of gum disease, like diabetes.

In some people, gingivitis progresses to periodontitis – with the destruction of the gingival fibers, the gum tissues become independent from the tooth and deepened sulcus, called a periodontal pocket. Sub gingival microorganisms (those that exist under the gum line) colonize the periodontal pockets and cause further inflammation within the gum tissues and progressive bone loss. samples of secondary causes are those things that, by definition, cause microbial plaque accumulation, like restoration overhangs and root proximity.

## 1.2 Gum arabic

Gum arabic, also called gum sudani, acacia gum, Arabic gum, gum acacia, acacia, gum arabic, Indian gum, and by other names,<sup>[14]</sup> can be a natural gum consisting of the hardened sap of two species of the acacia (sensu lato) tree, *Acacia Senegal*<sup>[15]</sup> (now called *Senegalia Senegal*) and *Vachellia (Acacia) seyal*. The term "gum arabic" doesn't indicate a specific botanical source. during an only a few cases, the so-called "gum arabic" may not even be collected from acacia species, but may originate from *Combretum*, *Albizia*, or another genus<sup>[14]</sup>.

### 1.2.1 Pharmacological potential

Gum arabic slows the speed of absorption of some drugs, including amoxicillin, from the gut. Nomadic populations of the Sahel and Arabia have known the beneficial effects of gum for ages. In Europe, pharmaceutical applications were also among the first uses<sup>[16]</sup>.

### 1.2.1.1 Antibacterial and Antifungal Activities:

A study was administrated to verify the antimicrobial activity. The results of study revealed that the extracts of stem bark have the antimicrobial property against *Streptococcus viridians*, *Staphylococcus aureus*, *E. coli*, *Bacillus subtilis* and *Shigella sonnei* using the agar diffusion method. *A. nilotica* (*A.arabica*) may well be a possible source of antimicrobial agents <sup>[17]</sup>. In another study within which Kalaivani and Methew reported that *A. nilotica* (*A.arabica*) demonstrates highest activity against three bacterial (*E. coli*, *S. aureus* and *Salmonella typhi*) and two fungal strain (*Candida albicans* and *Aspergillus niger*) <sup>[18]</sup>.

### 1.2.1.2 Antioxidant Activity

Scavenging activity of the bark powder extract in various solvents using maceration process was reported by Del WE <sup>[19]</sup>. Another study was allotted by Kalaivani T and Mathew L. They found that *A. nilotica* (*A.arabica*) is unquestionably accessible source of natural antioxidants, which could be used as a supplement to facilitate within the therapy of atom mediated diseases like cancer, diabetes, inflammation, etc. Furthermore, the high scavenging property of (*A.arabica*) could even be because of hydroxyl groups existing within the phenolic compounds which is able to scavenge the free radicals.

### 1.2.1.3 Antiviral Activity

Rehman et al reported th activity of *Acacia nilotica* (*A.arabica*) against viral hepatitis Virus in liver infected cells. The results explain that acetonic and methanolic extract of *Acacia arabica* (AN) showed quite 50% reduction in nontoxic concentration <sup>[20]</sup>.

### 1.2.1.4 Uses on oral and periodontal diseases

GA is taken under consideration to possess the pliability to spice up remineralization, due to its high concentration of calcium. A study was exhausted 2009 by Nor AL Huda, et al. among Sudanese school children, they studied caries experience and quantification of *Streptococcus mutants* and *Streptococcus sobrinus* in their Saliva, their results suggested that a regulation within the oral microflora may contribute to the prevention of caries they recommended employing a mix of probiotics and prebiotics as a preventive method <sup>[21]</sup>. it is also known that GA contains cyanogenetic glycosides and a number of other other different types of enzymes (such as oxidases, peroxidases and pectinases) that exhibit antimicrobial

Comment [u4]: Please revise the paragraph into more specific subject, related to your study

properties against certain organisms like Porphyromonas gingival and Prevotella intermedia<sup>[22]</sup>. Widespread of antibiotic resistance has been considering many antibiotics futile

against some important diseases, therefore there's an increased necessity not only to minimize antibiotic use and develop non-antibiotic based treatment but also to lift the profile of disease prevention<sup>[23]</sup>.

## **2. Material & method**

The present case-control study was carried out after getting approval from Institutional Ethical Committee and a consent form was signed by all patients. And the research was approved by the ethical committee of the Khartoum dental teaching hospital.

### **2.1 Material**

A pale white powder with particle size of 75-100 micron as readymade powder prepared by Sudanese Gum Arabic Board Riyadh, Khartoum State- Sudan.

### **2.2 Study design**

This study is A hospital-based double-blinded randomized parallel clinical trial using a split-mouth technique whose aim was to compare the effect of Acacia Arabica and distilled water in 88 sites of patients with chronic periodontitis who referred to department of Periodontology at the Khartoum Dental Teaching Hospital (KDTH), Khartoum, Sudan, during the period from July 2017 to December 2017 This study was approved in the ethics committee of information and research department at National Medicine and Poison Board (NMPB) and administrative authority of Khartoum dental teaching hospital (KDTH).

### **2.3 Study participants**

The participants of this study were adults of both sexes with the minimum of 20 teeth. All patients were recruited for this study population who met the following inclusion criteria patients diagnosed as chronic periodontitis according to American Academy of Periodontology (AAP 1999) were systemically healthy, with at least periodontal pockets  $\geq 4$ mm on both sites of the jaw.

## 2.4 Methodology

In this study the unit of comparison was quadrant (sites). The teeth of a total 44 patients were split into two parts. to represent a quadrant as the study group and the other on the other side are control group "88 sites. Periodontal measurement was performed in a dental chair by the candidate using a plain dental mirror and Williams marking periodontal probe to measure bleeding on probing (BOP), plaque index (PI) ,Gingival index (GI) the Probable pocket depth (PPD) were scored at six sites per tooth (mesio- buccal, mid- buccal, disto-buccal, mesio-lingual, mid-lingual, disto-lingual) as well as clinical attachment level (CAL) . simple random sampling technique was applied to select a representative study sample from the attending patients in Khartoum dental teaching hospital. Restricted randomization was used to allocate the GA and placebo irrigation to 44 participants, since the study was doubled blind, the trial principle examiner performed all clinical measurements and collected samples and for the immunological analysis, as well as the periodontal therapy while the irrigation (GA and DW irrigation) has been done by oriented general practitioner (other than the principal examiner) who had been trained to this practice, for the sleek of blinding. The study site was randomly selected for each group; they were randomly classified into two groups as follow using tossing a coin.

1. Experimental group (group A) study group who received gum arabic irrigation using Waterpik irrigator following the root surface debridement.
2. Control group (group B) control group who received distilled water (placebo) irrigation using Waterpik irrigator following the root surface debridement.

**Comment [u5]:** Please, delete the repeated words.

## 2.5 Study design

### 2.5.1 Gum Arabic as irrigation dosage

A concentration of 1 gram of gum arabic powder was prepared in 10 ml in distilled water then loaded in Waterpik model (made in the USA) irrigator —120 ml of gum arabic irrigation.

**Comment [u6]:** Mention the source of material (the company ,country)

### 2.5.2 Placebo formula

Distilled water irrigation using Waterpik irrigator, (Hydropulseur /irrigator) WP 360E2, ©2011 water Pik, Inc. designed in the USA, made in China. Following scaling and root

planning by Hand instruments scalers (Curettes) and Ultrasonic device (SATELEC, France) similar protocol for both intervention and placebo was followed.

### **2.5.3 Oral irrigation protocol**

Professional irrigation was done using Waterpik model Hydro pulseur irrigator WP-360E2. Waterpik 360 (8 ounces per min flow rate, 1450 pulse per min and 45 psi pressure) with a 120 ml reservoir was filled with either GA or DW. initially, the Waterpik jet stream was directed at a 90 angle to the gingival margin of the most posterior teeth for 30 second following scaling and root planning then suctioning and drying during the introduction of the intervention to avoid crossover effect of two interventions" contamination of two interventions". Every patient had received the same oral hygiene instructions and full mouth scaling and root planning. For each patient, we applied the two arms of intervention, GA, and DW for a period of one month a recall visit was scheduled every week with 10 min for single visit. Two teeth in opposite arch or cross arch were used for intervention and placebo. For the purpose of the blinding, the irrigation solution was applied by an oriented general practitioner on both sites (intervention and placebo).

GCF collection, periodontal examination and periodontal Treatment were done by the principal investigator, the measurements was done on the baseline before the examination and after one month using a dental mirror and William's marking periodontal probe, while the irrigation was done at day 0, 7, 15, 21 using the Waterpik irrigator every week for one month.

The pockets surround the teeth was measured at six surfaces (mid buccal, mesio buccal, distobuccally, mid lingual, mesiolingual and dentilingual) Clinical Attachment loss (CAL).

### **2.5.4 Measurement of GCF IL-1 $\beta$ level by ELISA**

The IL-1 $\beta$  level was assessed by Human IL-1 $\beta$  ELISA Kit (Human IL-1 $\beta$  ELISA MAX TM Deluxe set, Biolegend R, CA, USA) at day 0 and day 30 for all sites of interventions and placebo. Gingival crevicular fluid (GCF) sample has been collected to evaluate the proinflammatory interleukin 1 $\beta$  (IL-1 $\beta$ ) level from the periodontal pocket by using endodontic paper points size 30 (ZOGEAR Absorbent Paper Point 0.2 taper, Shanghai, China). From each participant, a total of 2 samples have been taken pre and post treatment. Total of 88 samples was been obtained from all participant. Cotton rolls and saliva ejector was used to prevent

contamination with saliva, following Brills techniques for collections GCF "the paper point had been inserted within the pocket until resistance is encountered and was left for 30 seconds, the samples were delivered into sterile cryogenic vial tube and stored at -80°C until IL1 $\beta$  analysis, as part of the protocol of institute of endemic disease laboratory. The GCF samples had been taken before the clinical measurement to avoid blood contamination and stimulating the GCF flow:

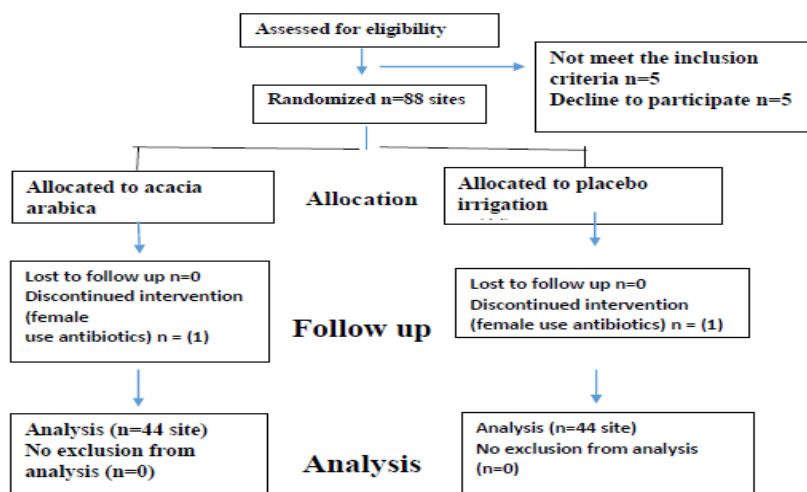


Fig.1 Consort flowchart study

### 2.3.4 Statistical analysis

Mean values in body weight and serum data were compared using SPSS version 22<sup>[24]</sup>.

## 3. Result

### 3.1 Periodontal parameters

The average value for PI, GI, PPD, CAL scores were obtained from the allocated sites score was present Table (1) during different time intervals for each group. At baseline, the mean PI of the interventional group was (2.23 ± 0.77) and for placebo group was (2.15 ± 0.73). By day 30 both

Comment [u7]: Needs more details

Comment [u8]: You have used many terms related to same study groups. Please specify one type only ,such as (control and experimental groups)



group had showed a decrease in PI mean ( $0.91 \pm 0.77$ ) and ( $1.0 \pm 0.84$ ) for the placebo group, both group showed a reduction in the PI mean from baseline that was statistically significant difference (P. value < 0.05). The GI mean showed ( $1.91 \pm 0.29$ ) for interventional group and ( $1.89 \pm 0.31$ ) for placebo group which presented a statistical significant difference by the end of the trial (P value < 0.05). The PPD mean as well showed ( $3.37 \pm 1.68$ ) at interventional group, where the placebo shows ( $3.32 \pm 1.65$ ) at baseline. Both group showed statistically significant difference (p.value <.05) Where the CAL mean in intervention and placebo was ( $3.81 \pm 2.67$ ), ( $3.82 \pm 2.22$ ) respectively which presented a statistical difference by the end of the trial (p.value <.05).

**Table No (1):** (Mean  $\pm$  SD) Of the Clinical Parameters

Group		Before		After		P value
		Mean $\pm$	SD mm	Mean $\pm$	SD mm	
<b>Intervention</b>	PI	2.23 $\pm$ 0.77		0.91 $\pm$ 0.77		0.001**
	GI	1.91 $\pm$ 0.29		0.57 $\pm$ 0.73		0.001**
	PPD	3.37 $\pm$ 1.68		2.55 $\pm$ 1.73		0.001**
	CAL	3.81 $\pm$ 2.67		2.98 $\pm$ 2.34		0.022*
<b>Placebo</b>	PI	2.15 $\pm$ 0.73		1.00 $\pm$ 0.84		0.001**
	GI	1.89 $\pm$ 0.31		0.61 $\pm$ 0.69		0.001**
	PPD	3.32 $\pm$ 1.65		2.51 $\pm$ 1.90		0.005**
	CAL	3.82 $\pm$ 2.22		3.21 $\pm$ 2.72		0.059

Values are means  $\pm$ SE, NS=not significant, \* Denotes mean values significant at (P<0.05), \*\*Significant=(P<0.01), \*\*\* Significant =(P<0.001).

bleeding on probing (BOP) before and after the intervention was present in table 2, the total number of sites with bleeding on probing was 41 before intervention and 3 has no BOP. After intervention 37 (90.2%) of them they have no BOP.

**Table No (2):** Shows Bleeding on probing before and after intervention

<b>Bleeding Intervention</b>	<b>After</b>	<b>No bleeding Intervention</b>	<b>After</b>	<b>Total</b>	<b>P. value</b>
<b>4</b>		<b>37</b>		<b>41 (probing)</b>	
<b>9.8%</b>		<b>90.2%</b>		<b>100.0%</b>	
<b>0</b>		<b>3</b>		<b>3</b>	
<b>0%</b>		<b>100%</b>		<b>100.0%</b>	<b>0.001</b>
<b>4</b>		<b>40</b>		<b>44 (placebo)</b>	
<b>9.1%</b>		<b>90.9%</b>		<b>100.0%</b>	

Values are means  $\pm$ SE, NS=not significant, \* Denotes mean values significant at (P<0.05), \*\*Significant= (P<0.01), \*\*\* Significant =(P<0.001).

The means $\pm$  standard deviations of GCF IL-1 $\beta$  before and after intervention were (148.9  $\pm$  79.7) and (98.00  $\pm$ 85.6) in intervention (P= 0.004) and (122.8  $\pm$ 79.2) and (113.1  $\pm$  88.2) in placebo (P= 0.586) and the level of both groups and correlation between IL1B and periodontal parameters presented in table (3).

**Comment [u9]:** No correlation was recorded between IL1 and periodontal parameters, so remove the sentence.

**Table No (3):** Mean  $\pm$  standard deviation of IL 1  $\beta$  level pretreatment and post-treatment of both groups

	<b>Before</b>			<b>After</b>			<b>Mean diff</b>	<b>P value</b>
	<b>Mean</b>	<b><math>\pm</math></b>	<b>SD</b>	<b>Mean</b>	<b><math>\pm</math></b>	<b>SD</b>		
<b>GA</b>	148.92	$\pm$	79.71	98.00	$\pm$	85.69	50.92	0.004**
<b>DW</b>	122.82	$\pm$	79.22	113.14	$\pm$	88.27	9.68	0.586

Values are means  $\pm$ SE, NS=not significant, \* Denotes mean values significant at (P<0.05), \*\*Significant= (P<0.01).

**Table No (4): Mean ± standard deviation of IL 1 β level pretreatment and post treatment of both groups**

**Comment [u10]:** Same results listed in table (3) so removed table(4)

	<b>Before</b>	<b>After</b>	<b>Mean diff</b>	
	<b>Mean ± SD</b>	<b>Mean ± SD</b>		<b>P value</b>
<b>Intervention</b>	148.92 ± 79.71	98.00 ± 85.69	50.92	0.004**
<b>Placebo</b>	122.82 ± 79.22	113.14 ± 88.27	9.68	0.586

Values are means ±SE, NS=not significant, \* Denotes mean values significant at (P<0.05), \*\*Significant= (P<0.01).

#### 4. Discussion

Periodontitis diagnosis and classification were established commonly on basis of clinical assessments (parameters), in spite of understanding of etiology and pathogenesis of periodontal destruction and assessment of the gingival health Armitage et al. [25] [26]. Most authors agreed that PI is (quantitative assessment) of plaque do not provide information regarding periodontal disease activity in specific sites, previous study that periodontitis is initiated in susceptible individuals by sub gingival plaque biofilm and that tissue destruction appears to be largely mediated by host response in specific bacteria and their product [27]. On the other hand, GI is also attributed to Löe and Sinless, which is assessing the severity of gingivitis based on color, consistency, and bleeding on probing. Furthermore, this study showed that there was a statistically significant reduction in both PI and GI after intervention in GA group (PI, GI with (P.value 0.001). A study conducted by Pradeep A. et al who used Acacia Arabica in the form of powder and gel in group of patients with chronic gingivitis the investigator found reduction in GI and PI scores by gum tone gel was significantly higher than the placebo gel group and similar to the chlorohexidine gel group and they claimed that the positive clinical effects of gum tone gel can be attributed to its main ingredients, such as Acacia Arabica [28]. In the present study all the participant had the same level of oral hygiene status at baseline due to effect of non-surgical periodontal therapy which would make the distinct improvement in PI and GI scores that documented in both groups after one month, however, the improvement was more evident among the group who received the GA irrigation compared to the control group who received the

placebo irrigation, The reduction in PI, GI readings in the control group could be ascribed to the mechanical effect of irrigator device or from Hawthorne effect which suggested that patients regularly appear to improve solely from the effects of being placed in clinical trial. <sup>[29]</sup><sup>[30]</sup>. On the other hand, also our study agrees with studies evoked by Tanged et al by using toothpaste containing Acacia Arabica and compares it to regular toothpaste. The study exhibited a clear reduction in PI and GI scores among the Acacia Arabica group compared with the regular toothpaste group and they suggested that using of AA in the formula of toothpaste may reduce the inflammation in gingivitis patients and regular brushing with Acacia Arabica can be recommended as an oral hygiene aid <sup>[31]</sup>. Furthermore, the result of the present study was not in accordance with the observation of Gazi who compared the effect of Acacia Senegal chewing gums as compared to sugar-free gum in a group of participant, the author found no statistically significant difference between two groups in PI and GI scores among the first group. This difference could be due to two different study populations or methods, Gazi in his study the population was a dental student with a high standard of oral hygiene. The difference could be due to the difference in the methodology they used. The short duration of the trial (one week) also could be a reason for a non-significant difference between the effects of intervention and control group. In the present study the statistically significant reduction of PI in the case group could be due to antimicrobial effect of Acacia Arabica which is supported by Clark et al.1993, who demonstrate the action of GA on the suppression of *P. gingivalis* and *p. intermedia* cultures and protease inhibitors activities. It was claimed that PPD reflects the damage to supporting structure while CAL reflects the cumulative effect on periodontal disease. In similar obtained by Ramesh Wari who found statistically significant difference in PPD ( $p < .05$ ) and CAL ( $p < .05$ ) reduction observed with use of *Acacia arabica gel* and they concluded that *Acacia Arabica leads to better clinical* outcomes in patients with mild to moderate chronic periodontitis. And they suggested that Greater reduction in PPD and CAL could be attributed to the antiprotease inhibition of *P. gingivalis* and *P. intermedia* by GA gel <sup>[32]</sup>. On the other hand, bleeding on probing (BOP) reflects histological, clinical and bacteriological alterations associated with periodontal disease <sup>[32]</sup>. In the present study, 41 of the participants had gingival bleeding before the intervention. After intervention 37 (i.e. 90.2%) of them did not present gingival bleeding, which indicated that, GA had a significant reduction in BOP% among this is patients similar to the findings reported by Tanged et al. and they were suggested that this reduction might be due

to astringent and anti-inflammatory effects of GA [33]. Furthermore, there is no participant develop bleeding after intervention so that the GA is biocompatible material and can be used for daily use without complication [34]. This Study was agreed with study obtained by Ghazala that compared Salivary Interleukin-1 $\beta$  and Matrix Metalloproteinase-8 Levels in Individuals with Chronic Periodontitis and found that this inflammatory marker was measured in patient's saliva again after 2 weeks and there was a reduction in their levels [35].

**Conclusion** This study concludes that the adjunctive use of a pulsating jet containing AA as an irrigation solution was efficient in reducing plaque index, gingival index, and BOP, PPD, CAL, as well as IL 1 $\beta$  level in subjects with chronic periodontitis.

## References

1. National Institute of Dental and Craniofacial Research. 2018 "Gum Disease". Retrieved 13 March 2018.
2. nhs.uk. Retrieved 2018 "Gum Disease Complications".
3. CDC. 10 March 2015 "Periodontal Disease". CDC. 10 March 2015. Retrieved 13 March 2018.
4. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators (October 2016). "Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015". *Lancet*. **388** (10053): 1545–1602. doi:10.1016/S0140-6736(16)31678-6. PMC 5055577. PMID 27733282.
5. Savage A, Eaton KA, Moles DR, Needleman I (June 2009). "A systematic review of definitions of periodontitis and methods that have been used to identify this disease". *Journal of Clinical Periodontology*. **36** (6): 458–67. doi:10.1111/j.1600-051X.2009.01408.x. PMID 19508246.
6. nhs.uk. Retrieved 2019 "Gum Disease Treatment". .
7. Mayo Clinic. Rochester, Minnesota 2018 "Gingivitis". : MFMER. 2017-08-04.
8. Crich A (June 1932). "Blastomycosis of the Gingiva and Jaw". *Canadian Medical Association Journal*. **26** (6): 662–5. PMC 402380. PMID 20318753.

**Comment [u11]:** Make sure your references are formatted correctly

9. Urzúa B, Hermosilla G, Gamonal J, Morales-Bozo I, Canals M, Barahona S, Cóccola C, Cifuentes V (December 2008). "Yeast diversity in the oral microbiota of subjects with periodontitis: *Candida albicans* and *Candida dubliniensis* colonize the periodontal pockets". *Medical Mycology*. **46** (8): 783–93. doi:10.1080/13693780802060899. PMID 18608938.
10. Matsuo T, Nakagawa H, Matsuo N (1995). "Endogenous *Aspergillus* endophthalmitis associated with periodontitis". *Ophthalmologica. Journal International d'Ophthalmologie. International Journal of Ophthalmology. Zeitschrift für Augenheilkunde*. **209** (2): 109–11. doi:10.1159/000310592. PMID 7746643.
11. Migliari DA, Sugaya NN, Mimura MA, Cucé LC (1998). "Periodontal aspects of the juvenile form of paracoccidioidomycosis". *Revista do Instituto de Medicina Tropical de Sao Paulo*. **40** (1): 15–8. doi:10.1590/S0036-46651998000100004. PMID 9713132.
12. Lalla E, Cheng B, Lal S, Kaplan S, Softness B, Greenberg E, Goland RS, Lamster IB (April 2007). "Diabetes mellitus promotes periodontal destruction in children". *Journal of Clinical Periodontology*. **34** (4): 294–8. doi:10.1111/j.1600-051X.2007.01054.x. PMID 17378885.
13. WebMD 2019 "Diabetes and Periodontal Disease". .
14. Mortensen, Alicja; Aguilar, Fernando; Crebelli, Riccardo; Di Domenico, Alessandro; Frutos, Maria Jose; Galtier, Pierre; Gott, David; Gundert Claude; Leblanc, Jean Oskarsson, Agneta; Parent Waalkens-Berendsen, Ine; Woutersen, Rudolf Antonius; Wright, Matthew; Younes, Maged; Brimer, Leon; Christodoulidou, Anna; Lodi, Federica; Tard, Alexandra; Dusemund, Birgit (2017). "Re-evaluation of gum (E 414) as a food additive". *EFSA Journal*. **15** (4): e04741. doi:10.2903/j.efsa.2017.4741. ISSN 1831-4732. PMC 7010027. PMID 32625453.
15. Eltayeb, IB; Awad, AI; Elderbi, MA; Shadad, SA (August 2004). "Effect of gum arabic on the absorption of a single oral dose of amoxicillin in healthy Sudanese volunteers". *The Journal of Antimicrobial Chemotherapy*. **54** (2): 577–8. doi:10.1093/jac/dkh372. PMID 15269196.

-Remy, Ursul  
-Charles; Lini  
-Massin,

**Comment [u12]:** Write 5 author's name only followed by et al.  
Alicja M, Fernando A, Riccardo C, Alessandro D, Maria Jose F, et al.


16. Dalen, van, Dorrit (2020). Gum Arabic. The Golden Tears of the Acacia Tree. Leiden: Leiden University Press. ISBN 9789087283360
17. Gilani A.H., Shaheen F., Zaman M., Janbaz K.H., Akhtar M.S., Shah B.H., (1999) Studies on antihypertensive and antispasmodic activities of methanol extract of *Acacia nilotica* pods, *Phytother Res*, 665-669.
18. Kalaivani T. and Methew L., (2010) Free radical scavenging activity from leaves of *Acacia nilotica* (L.) Wil. ex Delile, an Indian medicinal tree. *Food Chem. Toxicol.*, 298-305.
19. Del W.E. In vitro evaluation of peroxy radical scavenging capacity of water extract /fractions of *Acacia nilotica* (L.). *Afr. J. Biotechnol.* **8(7)**, 1270-1272 (2009)
20. Ashfaq U.A., Rehman S., Riaz S., Javed T. and Riazuddin S., Antiviral activity of *Acacia nilotica* against Hepatitis C Virus in liver infected cells, *Virology J.*, **8**, 220 (2011)
21. N.M.Nurelhuda MA-H, T.A. Trovik, V.Bakken *Caries* , 2010 Experience and Quantification of *Streptococcus mutans* and *Streptococcus sobrinus* in Saliva of Sudanese Schoolchildren. *Caries Res*; 44:402, 407
22. Aoba, T., 2004 Solubility properties of human tooth mineral and pathogenesis of dental caries, *Oral Dis*, 10, 249–257
23. DADaPD. M. 2009 Prospects for the development of probiotics and prebiotics for oral applications, *Journal of Oral Microbiology*,
24. Snedecor GW, Cochran WC. *Statistical methods*, 8th Edn, Iowa State University Press, Ames, Iowa; 1989.
25. Armitage, G.C., *Clinical evaluation of periodontal diseases*, *Periodontology* 2000, 1995. 7(1): p. 39-53.
26. Ryan RJ, The accuracy of clinical parameters in detecting periodontal disease activity. *The Journal of the American Dental Association*, 1985,111(5):753-60.
27. Matthews, J., et al., Hyperactivity and reactivity of peripheral blood neutrophils in chronic periodontitis, *Clinical & Experimental Immunology*, 2007. 147(2): p. 255-264.
28. Pradeep A, Happy D, Garg G. Short - term clinical containing *Acacia arabica*: a randomized controlled clinical trial. *Australian dental journal*, 2010; 55(1):65-9.

Comment [u13]: Write volume and number

29. McCartney, R., et al., The Hawthorne Effect: a randomized, controlled trial. BMC, Medical research methodology, 2007,7(1): p. 30.
30. Wickström, G. and T. Bendix, the" Hawthorne effect —what did the original Hawthorne studies actually show, *Scandinavian journal of work, environment & health*, 2000: p. 363-367.
31. Tangade PS MA, Tirth A, Kabasi S. Anti-gingivitis effects of Acacia arabicacontaining toothpaste. Chin J Dent Res. 2012; 15(1):49-53.
32. Singhal R, Agarwal V, Rastogi P, Khanna R, Tripathi S. Efficacy of Acacia arabica gum as an adjunct to scaling and root planing in the treatment of chronic periodontitis: A randomized controlled clinical trial, The *Saudi Dental Journal*. 2017.
33. El Din AGS, Zarroug Production andcommercialization of gum arabic in Sudan, Domestication and commercialization of non-timber forest products. 1996,176.
34. Doi, Y., et al., A ninety-day oral toxicity study of a new type of processed gum arabic, from Acacia tree (Acacia senegal) exudates, in F344 rats. Food and chemical toxicology, 2006. 44(4): p. 560-566.

Comment [u14]: Write volume and number

Comment [u15]: Write volume and number

- Ghazala Hassan, Comparison of Salivary Interleukin-1 $\beta$  and Matrix Metalloproteinase-8 Levels in Individuals with Chronic Periodontitis. *ClinicalTrials.gov* Identify
35. : 2017.

Comment [u16]: Write volume and number